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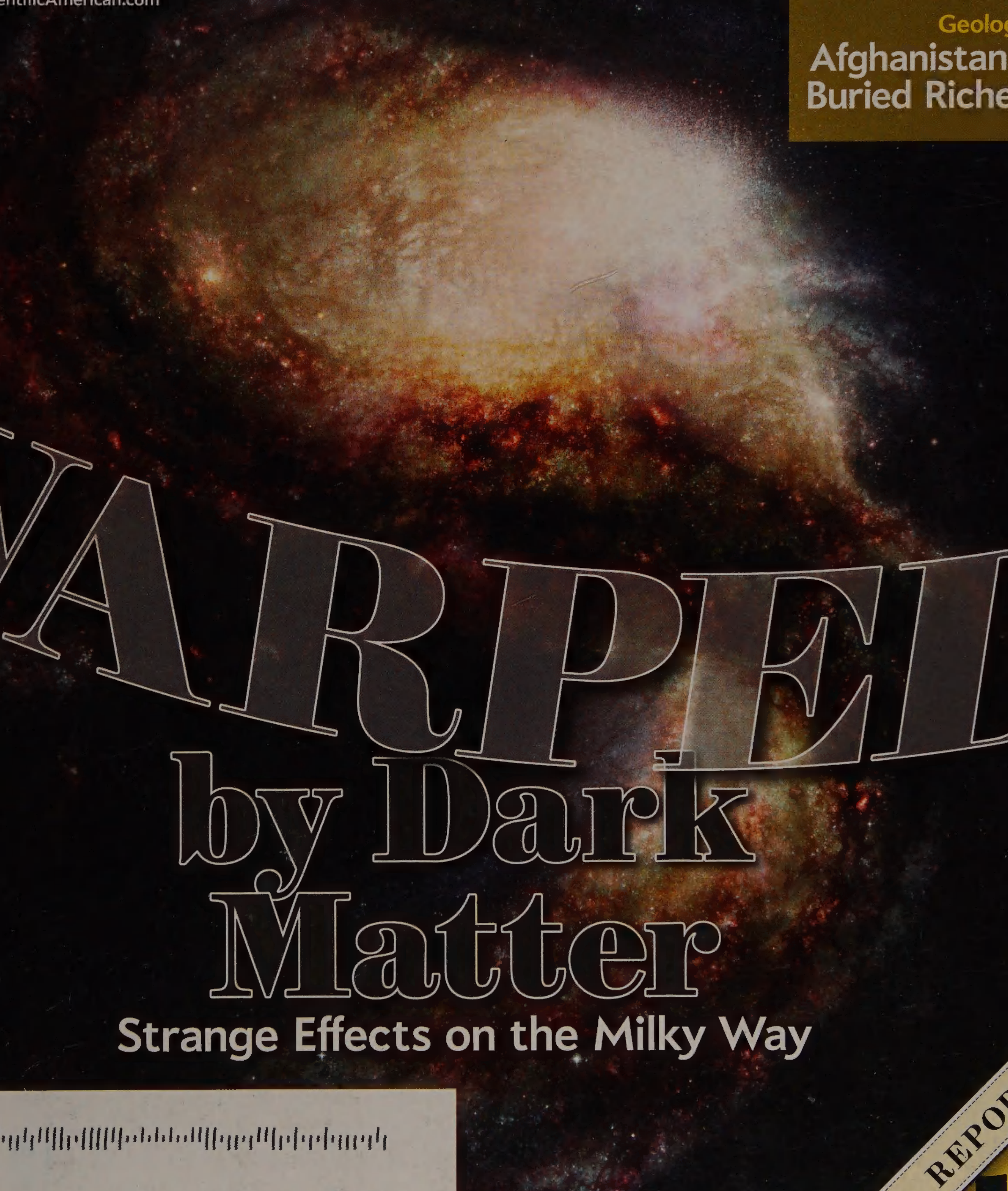
Geology
Afghanistan's Buried Riches



WARPED by Dark Matter

Strange Effects on the Milky Way

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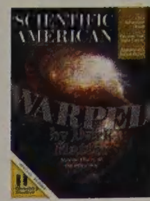
SCIENTIFIC AMERICAN

Volume 305, Number 4

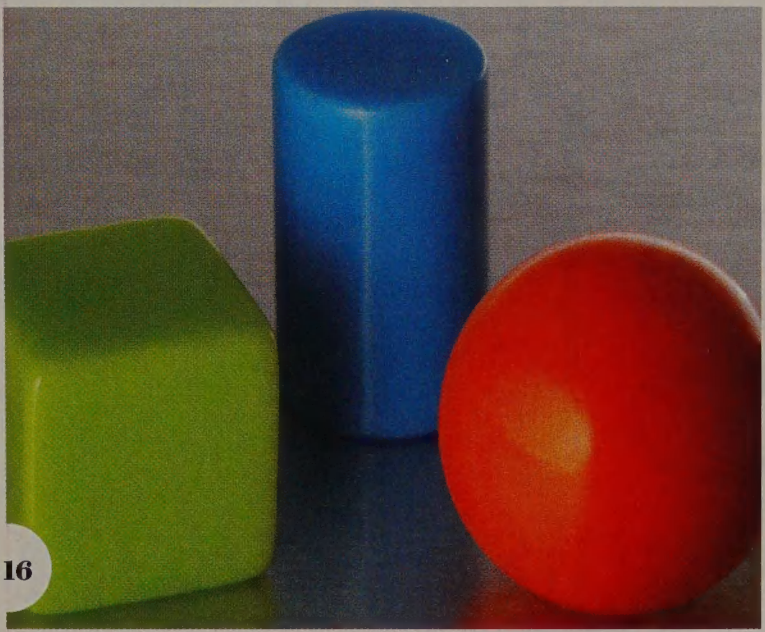
ON THE COVER

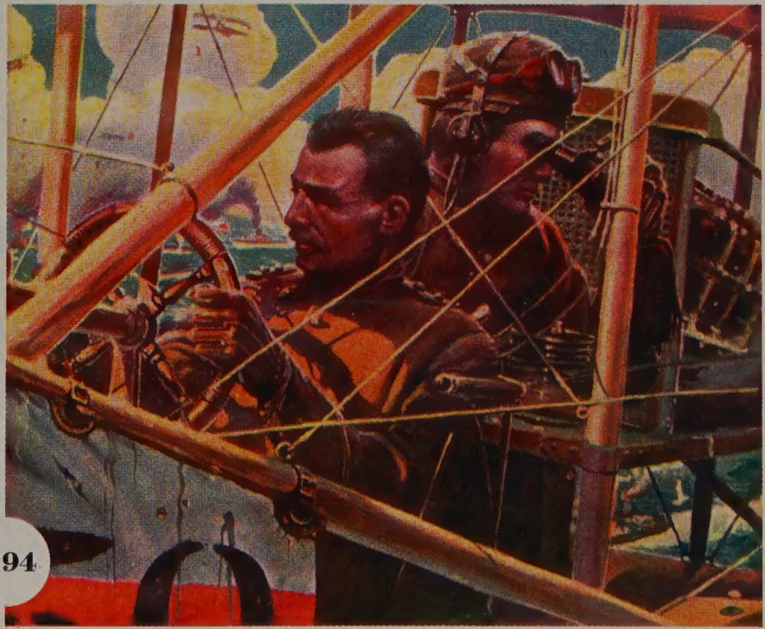


It's warped! The Milky Way galaxy, often depicted as a flat disk containing a spiral pattern of stars and gas, actually has a notable twist. The warp baffled astronomers until they realized that dark matter might form clumps and wrest the galactic disk into this shape. Dark matter also makes sense of other puzzles of our cosmic neighborhood.
Image by Kenn Brown, Mondolithic Studios.

FEATURES

Photograph by Dan Saelinger





SCIENTIFIC AMERICAN

DEPARTMENTS

ON THE WEB

Ten Years after 9/11

A decade after the terrorist attacks on New York City and Washington, D.C., how have passenger-screening systems, surveillance networks and military technologies evolved? And what vulnerabilities remain?
Go to www.ScientificAmerican.com/oct2011/terrorism

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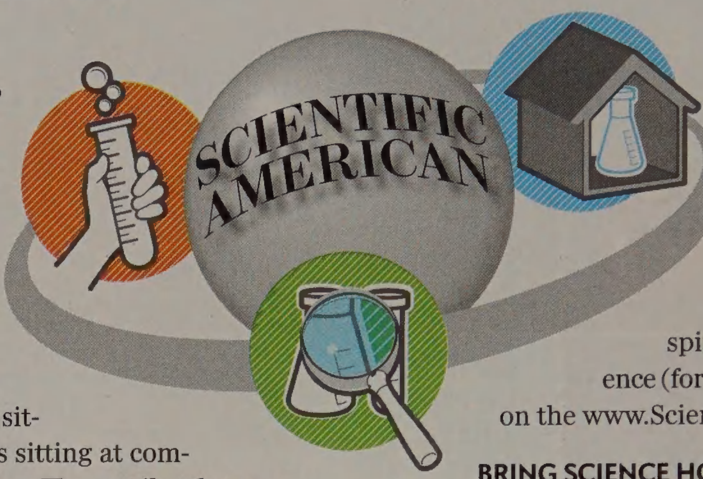
Mariette DiChristina is editor in chief of *Scientific American*. Find her on Twitter @SAeditorinchief

Back to School



AROUND THE TIME YOU READ this, the popular Introduction to Artificial Intelligence course at Stanford University, taught by Sebastian Thrun, director of the AI lab there, and by Peter Norvig, director of research for Google, will be under way. As usual, a couple of hundred Stanford students will be sitting in the room. This year classmates sitting at computers around the world will join them. The pupils who attend virtually won't pay tuition (or get Stanford credit), but they will all watch the same lectures, read the same textbook, get the same homework and take the same tests. Software will help analyze their submitted questions, so that the professors can address the main themes each week.

I spoke to Norvig while attending the recent Sci Foo—an invitation-only "unconference" hosted by Google, the O'Reilly Media Group and Nature Publishing Group (*Scientific American*'s parent company). Just two weeks after he and Thrun announced the AI course, more than 57,000 students had enrolled (70,000-plus at press time). "We hope our automated systems hold up," he joked.

Sci Foo hosts scientists and technologists from many fields, who create the session schedule during the conference rather than beforehand. This year finding exciting new approaches to improve education was a frequent theme—and those sessions were packed. (Linda Rosen, CEO of Change the Equation, and I ran one, on how to inspire kids about science.)

On the topic of education, here are three updates on *Scientific American*'s efforts to inspire by expanding the reach of science (for more, click on the "Education" tab on the www.ScientificAmerican.com home page):

BRING SCIENCE HOME. Following our successful weekday series of science activities for parents and kids ages six to 12, which ran through May, we will post more fun projects, starting in October.

1,000 SCIENTISTS IN 1,000 DAYS. In May we invited scientists, engineers, mathematicians, doctors and others to volunteer to visit classrooms as part of our three-year (that's the 1,000 days) Change the Equation program. More than 1,100 have stepped forward—in fewer than 100 days—and they are in a variety of disciplines and located all around the country. This fall we plan to offer a service that connects these scientists with educators.

CITIZEN SCIENCE. One of the best ways to appreciate science, of course, is to participate in it yourself. Working with Zooniverse and a researcher at the Woods Hole Oceanographic Institute, we are launching a project that lets students and adults alike help study whale songs.

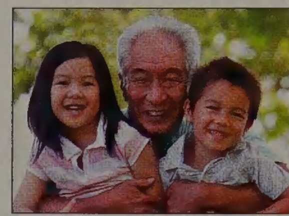
How else can we engage kids in science? As always, we welcome your thoughts. ■

Illustration by Nick Higgins

PET brain scan images (color) overlay MRI images (gray) to provide a comprehensive view of the brain's health. The upper row shows brain changes associated with normal aging. The lower row shows the onset of dementia, one form of which is Alzheimer's disease. Orange-to-yellow coloring indicates regions with reduced glucose metabolism.

Helping to make better diagnoses

Positron Emission Tomography (PET) may become an even more powerful tool for distinguishing between normal aging and dementia, such as Alzheimer's disease — thanks to a unique database and analytics being developed by Hamamatsu.



For a number of years Hamamatsu has been building an unusual database. We now have PET brain scans from over 6,000 *normal, healthy individuals,* both men and women, in a wide range of ages. And our researchers have learned a lot about how healthy brains look and how they change over time.

So, in the future, doctors may be able to spot

Hamamatsu is opening the new frontiers of Light ✳✳✳

more subtle anomalies in brain health by comparing their patients' PET scans with Hamamatsu's database — specifically by sex and age!

Hamamatsu's aim is to provide clinicians with new tools, to help them distinguish more clearly between normal aging and the early stages of dementia. Because earlier diagnoses may give doctors more options for treatment.

And though there are no cures for Alzheimer's disease at present, starting treatment earlier may give patients and their caregivers precious extra time to enjoy their quality of life.

It's one more way Hamamatsu is opening the new frontiers of light to improve our world.

http://jp.hamamatsu.com/en/rd/publication/

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June 2011

STICKING TO CLIMATE SCIENCE

As an undergraduate physics major in the mid-1980s at the University of California, Berkeley, I knew about Richard Muller—the physics professor who was the subject of Michael D. Lemonick's interview, "'I Stick to the Science'"—and his controversial theory that a "death star" was responsible for major mass extinctions. Later, as a graduate student studying climate, I became aware of Muller's work attempting to overthrow the traditional Earth orbital theory of the ice ages—that, too, didn't pan out. To be clear, there is nothing wrong in science with putting forth bold hypotheses that ultimately turn out to be wrong. Indeed, science thrives on novel, innovative ideas that—even if ultimately wrong—may lead researchers in productive new directions.

One might hope, however, that a scientist known for big ideas that didn't stand the test of time might be more circumspect when it comes to his critiques of other scientists. Muller is on record accusing climate scientists at the University of East Anglia Climatic Research Unit of hiding data—a charge that was rejected in three separate investigations. In his interview, Muller even maligned my own work on the "hockey stick" reconstruction of past temperatures. He falsely claimed "the hockey-stick chart was in fact incorrect" when in fact the National Academy of Sciences affirmed our findings in a major 2006 report that *Nature* summarized as "Academy affirms hockey-stick graph." *Scientific American* itself recently ran an article it billed as "Novel analysis confirms climate 'hockey stick' graph" ["Still Hotter Than Ever," by David Appell, News Scan; Scientific American, November 2009].

Rather than providing a platform for Muller to cast aspersions on other scientists, Lemonick could have sought some introspection from him. How, for example, have the lessons learned from his past failures influenced the approach he has taken in his more recent forays into the science of human-caused climate change? More than anything else, the interview was simply a lost opportunity. Not only can *Scientific American* do better, it will need to.

Michael E. Mann
Pennsylvania State University

"One has to weigh the benefits of ethical meat versus the dangers of generating antibiotic-resistant bacteria."

LOUIS DE LÉSÉLEUC
NATIONAL RESEARCH COUNCIL CANADA

NO DEFENSE

"Inside the Meat Lab," by Jeffrey Bartholet, failed to point out one major issue. Unlike animals, the bioreactor-based meat he proposes does not have an immune system. Hence, the nutrient-rich cell-growth systems would have to be run in a completely microbe-free environment, significantly raising costs. A single contaminant could ruin tons of meat products. If the solution is to introduce antibiotics, then one has to weigh the benefits of mass-producing ethical meat against the dangers of generating antibiotic-resistant bacteria—an all too familiar dilemma.

Louis de Léséleuc
Infections and Immunity Group
National Research Council Canada

PROTEST TARGET'S RESPONSE

"Quotable" [Advances] took a line out of context from an editorial I wrote for the newspaper of the American College of Surgeons concerning new findings in the biochemistry of semen. Research had shown that the seminal fluid might have mood-enhancing effects on women after unprotected sex and promote stronger bonding between partners—a gift from nature. The lighthearted comment you quoted (that it may be a better Valentine's gift than chocolate) amused most readers of the newspaper but irritated others. Despite my apologies and resignation as editor, a group of women threatened to protest at any medical meeting I attended, so I resigned as president-elect of the organization. Steven M. Platek, co-author of the semen study, commented: "How can someone be asked to resign for citing a peer-reviewed paper? Dr. Greenfield was forced to resign based on politics, not evidence. His resignation is more a reflection of the feminist and antiscientific attitudes of some self-righteous and indignant members of the American College of Surgeons. Science is based on evidence, not politics. In science, knowing is always preferable to not knowing."

It also helps to know the whole story.

Lazar J. Greenfield
Professor emeritus of surgery
University of Michigan at Ann Arbor

CONSCIOUS EFFORTS

Christof Koch and Giulio Tononi ["A Test for Consciousness"] defined an experimental method that seems likely to improve significantly on the Turing test as a way to operationally define and identify "intelligence." The use of sensible versus nonsensical composite images would surely pose challenges to machines—today and for the foreseeable future. I think the article has two weaknesses, however. First, I think the authors underestimate the rate of progress that artificial intelligence will make in this area if it is deemed important. As they point out, the human ability to discern implausible relationships is based on a vast amount of knowledge acquired from experience. The foundations for giving machines that experience have been under development for decades and are gaining traction in many application areas today. It would be silly to take on faith that these tasks are fundamentally or nearly beyond what machines can do.

The second weakness, in my opinion,

is that it confuses consciousness with integrated knowledge. Requiring machines to demonstrate that they understand visual elements and relationships seems a straightforward and appropriate aspect of intelligence. But it does not mean that any machine that exhibited that kind of perceptual and cognitive capability would obviously be conscious.

At its core, consciousness is a term we use to refer to our common human perception that we exist, are aware of ourselves and are aware of our being part of the environment with which we are interacting. Self-awareness and awareness of self versus our environment would seem to be important attributes of consciousness, regardless of how it might ultimately be defined and identified. The authors' proposed test neither depends on those attributes nor distinguishes those having them from those lacking them.

RICK HAYES-ROTH
Professor of information systems
Naval Postgraduate School

OUR QUANTUM WORLD

In "Living in a Quantum World," Vlatko Vedral insists that "quantum mechanics is not just about teeny particles. It applies to things of all sizes: birds, plants, maybe even people." But all his examples of entanglement refer to the teeny particles—atoms and molecules. The fact that, in some examples, the entangled particles are located within organisms—birds, plants—does not prove that these organisms themselves are entangled. Do the particles and the bodies behave according to the laws of quantum mechanics? Vedral's answer is affirmative. But that something appears that way to the author and his colleagues is not a sufficient base for sweeping generalizations.

ALEXANDER YABROV
Princeton, N.J.

ERRATUM

Jeffrey Bartholet wrote in "Inside the Meat Lab" that Willem van Eelen and H. P. Haagsman published "the first peer-reviewed article on cultured meat in the journal *Tissue Engineering*." The sentence should have read: "the first peer-reviewed article on the prospects for industrial production of cultured meat."

Winner of the 2011 National Magazine Award for General Excellence

Ban Chimp Testing

Why it is time to end invasive biomedical research on chimpanzees

The testing began shortly after Bobby's first birthday. By the time he was 19 he had been anesthetized more than 250 times and undergone innumerable biopsies in the name of science. Much of the time he lived alone in a cramped, barren cage. Bobby grew depressed and emaciated and began biting his own arm, leaving permanent scars.

SUZI ESZTERHAS *Getty Images*

Bobby is a chimpanzee. Born in captivity to parents who were also lab chimps, he grew up at the Coulston Foundation, a biomedical research facility in Alamogordo, N.M., that was cited for repeated violations of the Animal Welfare Act before it was shuttered in 2002. He is one of the lucky ones. Today he lives in a sanctuary called Save the Chimps in Fort Pierce, Fla., where he can socialize and roam freely. Last year the National Institutes of Health announced plans to put some 180 ex-Coulston chimps currently housed at the Alamogordo Primate Facility back in service, to rejoin the roughly 800 other chimps that serve as subjects for studies of human diseases, therapies and vaccines in the U.S., which is the only country apart from Gabon to maintain chimps for this purpose.

Public opposition is on the rise. In April a bipartisan group of senators introduced a bill, the Great Ape Protection and Cost Savings Act, to prohibit invasive research on great apes, including chimps. And when the NIH announced its plans for bringing the Alamogordo chimps out of retirement, objections from the Humane Society, primatologist Jane Goodall and others prompted the agency to put the plans on hold until the Institute of Medicine (IOM) completes a study of whether chimps are truly necessary for biomedical and behavioral research. The IOM project itself has been criticized: the NIH instructed it to omit ethics from consideration.

In April, McClatchy Newspapers ran a special report based on its review of thousands of medical records detailing research on chimps like Bobby. The stories painted a grim picture of life in the lab, noting disturbing psychological responses in the chimps. Then, in June, Hope R. Ferdowsian of George Washington University and her colleagues reported in *PLoS ONE* that chimps that had previously suffered traumatic events, including experimentation, exhibit clusters of symptoms similar to depression and post-traumatic stress disorder in humans.

That chimps and humans react to trauma in a like manner should not come as a surprise. Chimps are our closest living relatives and share a capacity for emotion, including fear, anxiety, grief and rage.

Testing on chimps has been a huge boon for humans in the past, contributing to the discovery of hepatitis C and vaccines against polio and hepatitis B, among other advances. Whether it will continue to bear fruit is less certain. Alternatives are emerging, including ones that rely on computer modeling and isolated cells. In 2008 pharmaceutical manufacturer GlaxoSmithKline announced it would end its use of chimps.

In our view, the time has come to end biomedical experimentation on chimpanzees. The Senate bill would phase out invasive research on chimps over a three-year period, giving the researchers time to implement alternatives, after which the animals would be retired to sanctuaries.

We accept that others may make a different moral trade-off. If the U.S. elects to continue testing on chimps, however, then it needs to adopt stricter guidelines. Chimps should be used only in studies of major diseases and only when there is no other option. Highly social by nature, they should live with other chimps and in a stimulating environment with room to move around. And when a test inflicts pain or psychological distress, they should have access to treatment that eases those afflictions.

The Animal Welfare Act affords chimps some protection. But clearly more is needed. To develop and enforce tighter regulations, the U.S. Department of Agriculture, which enforces the Animal Welfare Act, should establish an ethics committee specifically for biomedical research on chimps. The committee would need to include not just medical researchers but also bioethicists and representatives from animal welfare groups. Such measures would no doubt make medical testing on chimps even more expensive than it already is. Yet if human lives are going to benefit from research on our primate cousins, it is incumbent on us to minimize their suffering, provide them with an acceptable quality of life—and develop techniques that hasten the day when all of Bobby's fellow chimps can join him in retirement.

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/oct2011

Patricia Hunt is professor of genetics in the School of Molecular Biosciences at Washington State University, Pullman.

Toxins All around Us

Exposure to the chemicals in everyday objects poses a hidden health threat

Susan starts her day by jogging to the edge of town, cutting back through a cornfield for an herbal tea at the downtown Starbucks and heading home for a shower. It sounds like a healthy morning routine, but Susan is in fact exposing herself to a rogue's gallery of chemicals: pesticides and herbicides on the corn, plasticizers in her tea cup, and the wide array of ingredients used to perfume her soap and enhance the performance of her shampoo and moisturizer. Most of these exposures are so low as to be considered trivial, but they are not trivial at all—especially considering that Susan is six weeks pregnant.

Scientists have become increasingly worried that even extremely low levels of some environmental contaminants may have significant damaging effects on our bodies—and that fetuses are particularly vulnerable to such assaults. Some of the chemicals that are all around us have the ability to interfere with our endocrine systems, which regulate the hormones that control our weight, our biorhythms and our reproduction. Synthetic hormones are used clinically to prevent pregnancy, control insulin levels in diabetics, compensate for a deficient thyroid gland and alleviate menopausal symptoms. You wouldn't think of taking these drugs without a prescription, but we unwittingly do something similar every day.

An increasing number of clinicians and scientists are becoming convinced that these chemical exposures contribute to obesity, endometriosis, diabetes, autism, allergies, cancer and other diseases. Laboratory studies—mainly in mice but sometimes in human subjects—have demonstrated that low levels of endocrine-disrupting chemicals induce subtle changes in the developing fetus that have profound health effects in adulthood and even on subsequent generations. The chemicals an expecting mother takes into her body during the course of a typical day may affect her children and her grandchildren.

This isn't just a lab experiment: we have lived it. Many of us born in the 1950s, 1960s and 1970s were exposed in utero to diethylstilbestrol, or DES, a synthetic estrogen prescribed to pregnant women in a mistaken attempt to prevent miscarriage. An article in the June issue of the *New England Journal of Medicine* called the lessons learned about the effects of fetal human exposures to DES on adult disease "powerful."

In the U.S., two federal agencies, the Food and Drug Administration and the Environmental Protection Agency, are responsible for banning dangerous chemicals and making sure that chemicals in our food and drugs have been thoroughly tested. Scientists and clinicians across diverse disciplines are concerned that the efforts of the EPA and the FDA are insufficient in the face of the complex cocktail of chemicals in our environment. Updating a proposal from last year, Senator Frank R. Lautenberg of New Jersey introduced legislation this year to create the Safe Chemicals Act of 2011. If enacted, chemical companies would be required to demonstrate the safety of their products *before* marketing them. This is perfectly logical, but it calls for a suitable screening-and-testing program for endocrine-disrupting chemicals. The need for such tests has been recognized for more than a decade, but no one has yet devised a sound testing protocol.

Cuppa disrupters: Chemicals in disposable cups may mimic hormones.

PETER DAZELEY *Getty Images*

Regulators also cannot interpret the mounting evidence from laboratory studies, many of which use techniques and methods of analysis that weren't even dreamed of when toxicology testing protocols were developed in the 1950s. It's like providing a horse breeder with genetic sequence data for five stallions and asking him or her to pick the best horse. Interpreting the data would require a broad range of clinical and scientific experience.

That's why professional societies representing more than 40,000 scientists wrote a letter to the FDA and EPA offering their expertise. The agencies should take them up on it. Academic scientists and clinicians need a place at the table with government and industry scientists. We owe it to mothers everywhere, who want to give their babies the best possible chance of growing into healthy adults.

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/oct2011

ADVANCES

Dispatches from the frontiers of science, technology and medicine

BIOLOGY

More Than Child's Play

Young children think like researchers but lose the feel for the scientific method as they age

If your brownies came out too crispy on top but undercooked in the center, it would make sense to bake the next batch at a lower temperature, for more time or in a different pan—but not to make all three changes at once. Realizing that you can best tell which variable matters by altering only one at a time is a cardinal principle of scientific inquiry.

Since the 1990s studies have shown that children think scientifically—making predictions, carrying out mini experiments, reaching conclusions and revising their initial hypotheses in light of new evidence. But while children can play in a way that lets them ascertain cause and effect, and even though they have a rudimentary sense of probability (eight-month-olds are surprised if you reach into a bowl containing four times as many blue marbles as white ones and randomly scoop out a fistful of white ones), it was not clear whether they have an implicit grasp of a key strategy of experimental science: that by isolating variables and testing each independently, you can gain information.

To see whether children understand this concept, scientists at the Massachusetts Institute of Technology and Stanford University presented 60 four- and five-year-olds with a challenge. The researchers showed the kids that certain plastic beads, when placed individually on top of a special box, made green LED lights flash and music play. Scientists then took two pairs of attached beads, one pair glued together and the other separable, and demonstrated that both pairs activated the machine when laid on the box. That raised the possibility that only one bead in a pair worked. The children were then left alone to play. Would they detach the separable pair and place each bead individually on the machine to see which turned it on?

They did, the scientists reported in September in the journal *Cognition*. So strong was the kids' sense that they could only figure out the answer by testing the components of a pair independently that they did something none of the scientists expected: when the pair was glued together, the children held it vertically so that only one bead at a time touched the box. That showed an impressive determination to isolate the causal variables, says Stanford's Noah Goodman: "They actually designed an experiment to get the information they wanted." That suggests basic scientific principles help very young children learn about the world.

The growing evidence that children think scientifically presents a conundrum: If even the youngest kids have an intuitive grasp of the scientific method, why does that understanding seem to vanish within a few years? Studies suggest that K–12 students struggle to set up a controlled study and cannot figure out what kind of evidence would support or refute a hypothesis. One reason for our failure to capitalize on this scientific intuition we display as toddlers may be that we are pretty good, as children and adults, at reasoning out puzzles that have something to do with real life but flounder when the puzzle is abstract, Goodman suggests—and it is abstract puzzles that educators tend to use when testing the ability to think scientifically. In addition, as we learn more about the world, our knowledge and beliefs trump our powers of scientific reasoning. The message for educators would seem to be to build on the intuition that children bring to science while doing a better job of making the connection between abstract concepts and real-world puzzles. *—Sharon Begley*

CHRIS COLLINS *Getty Images*

FURTHER READINGS AND CITATIONS ScientificAmerican.com/oct2011/advances

ENVIRONMENT

Is It Safe to Drink?

The government may not be doing enough to regulate contaminants in tap water

More than 6,000 chemicals pollute U.S. drinking water, yet the U.S. Environmental Protection Agency has added only one new pollutant to its regulatory roster in the past 15 years. Environmental groups have long raised questions about this track record, and the U.S. Government Accountability Office recently joined the chorus, releasing a report that charges the agency with taking actions that have "impeded ... progress in helping assure the public of safe drinking water."

Among other things, the GAO report says, the EPA relies on flawed data. To determine the level of a particular pollutant in drinking water—which the EPA does before making a regulatory ruling on it—the agency relies on analytic testing methods so insensitive that they cannot identify the contaminants at levels expected to cause health effects. In addition, since 1996 the EPA has been required to make regulatory decisions about five new pollutants each year, ruling on those that might pose the biggest threats to public health. The GAO report asserts that the agency has been ruling only on the "low-hanging fruit"—contaminants for which regulatory decisions are easy rather than those that might be the most dangerous. "They're not actually doing anything to protect public health," says Mae Wu, an attorney at the Natural Resources Defense Council.

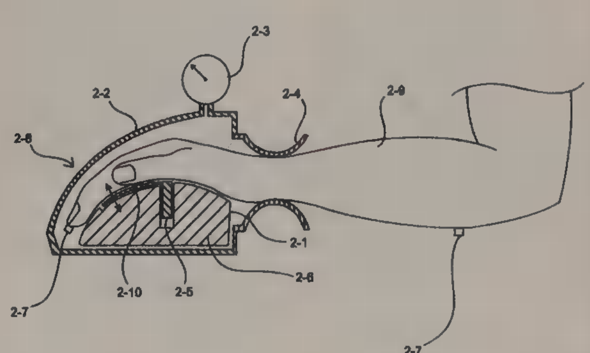
For its part, the EPA has pledged to review the nation's drinking-water standards and to add at least 16 new contaminants to the list of those it regulates. This past February the agency reversed a longstanding decision to not regulate the rocket-fuel ingredient perchlorate, making the chemical the first new drinking-water contaminant to be regulated since 1996. In its response to the GAO, the EPA stated that "no action" was necessary to better prioritize the contaminants on which the agency will rule in the future, nor did it acknowledge the need for improvements in data collection. The agency did, however, agree to consider improving its methods for alerting the public when there are drinking-water advisories.

—Melinda Wenner Moyer

PATENT WATCH

Controlled heat transfer with mammalian bodies: In the 1990s Stanford University biologists Dennis Grahn and H. Craig Heller discovered a novel way of treating patients with a condition known as postanesthetic hypothermia, in which patients emerging from anesthesia are so cold that they shiver for up to an hour. The condition develops in part because anesthesia reduces the body's ability to control its own temperature. Applying heat alone does not always help, so Grahn and Heller tried another approach: they increased the volume of blood flowing to the skin of patients' hands and then applied heat to the same area. "These people were fine within 10 minutes," Grahn says. "Then the question was, 'What the heck is going on here?'"

They had stumbled on a feature of mammalian biology that can be manipulated for a wide array of other applications, including ones requiring cooling. Among these uses is increasing athletic endurance, because overheating is one of the primary factors limiting physical performance. One of the main ways the human body regulates internal temperature is by controlling the amount of blood flow through nonhairy skin areas, such as the palms, the cheeks, the nose and the soles of the feet. Underneath the skin of these areas are unique vascular structures designed to deliver large volumes of blood to the surface. When the body needs to release heat, it expands these vessels and floods the area with blood, throwing off heat through the skin. The body holds in heat by constricting blood flow to these areas.



Patent No. 7,947,068 outlines a variety of ways to manipulate these processes. One, called the Glove, is already in use by the San Francisco 49ers. Players stick their hand into the coffeepot-size device, which creates an airtight seal around the wrist. The Glove then uses a pressure differential to draw blood to the palm and rapidly cool it, which leads to an overall decrease in body temperature. The device can be used at any point during a game and takes only a few minutes to work. Tests in the lab, Grahn says, have shown that devices like the Glove can dramatically increase athletic output and reduce heat stress. *—Adam Piore*

GALLERY STOCK (*top*); COURTESY OF U.S. PATENT AND TRADEMARK OFFICE (*bottom*)

WHAT IS IT?

Disguise genes: Many animals fool predators by changing colors to mimic their surroundings or the traits of other species. Two teams recently identified genes that control this process in a large genus of tropical butterflies known as *Heliconius.* Several *Heliconius* species evolved a similar array of patterns over thousands of years despite their varying geographic locations. One study found 18 genes regulate seven different wing patterns, which warn birds of the butterflies' toxicity. Another study described a single gene's control of the red patterns on many species (including *H. erato,* magnified 15 times at the right). Arnaud Martin, a University of California, Irvine, graduate student involved in this research, says the work helps to explain "how changes in DNA can generate new features such as a bigger brain, an oppositional thumb [or] a colorful butterfly." —*Ann Chin*

COURTESY OF ARNAUD MARTIN *University of California, Irvine*

PROFILE

NAME
Brent Stockwell

TITLE
Associate professor, Columbia University

Early career scientist, Howard Hughes Medical Institute

LOCATION
New York City

FIELD NOTES

Outsmarting Cancer

A biologist talks about what makes disease-causing proteins so difficult to target with drugs

There really is a crisis now occurring in the pharmaceutical industry. For the past 10 to 15 years the number of new drugs has been declining because it's becoming harder and harder to create new medicines.

A lot of people have speculated about why. One explanation I support is that we've run out of proteins that can be targeted with drugs. The targets that are left are "undruggable."

Proteins that are considered undruggable don't have large pockets or cavities inside them and instead are relatively flat on their surfaces. There's no obvious site for a small molecule, a therapeutic candidate, to interact. Fifteen percent of proteins are considered druggable. What percent of proteins modify disease? It might be somewhere around 10 to 15 percent. There's no correlation between whether a protein is druggable and whether it's disease-modifying. Most proteins that drive disease processes are actually undruggable.

The reason I wrote *The Quest for the Cure* [Columbia University Press, 2011] was that I thought this was an important problem that most people are not aware of—even in science, let alone the general public. And if we can get the best minds to tackle this question, I am optimistic that we will ultimately be successful in finding solutions to most, if not all, of these proteins.

In my lab, our goal is to find proteins that control cell-death mechanisms in cancer and neurodegenerative diseases and then to find small molecules that can inhibit or activate those proteins.

We're at a relatively early stage, but we have tried to target one class of proteins called E3 ligases, which are involved in pretty much every disease and cellular process. They have been considered undruggable, however, because there are no small molecules that can block their activity. Our strategy was to model, on a computer, the way a small molecule interacts with a particular E3 ligase and to predict small molecules that might interact favorably. Then we picked the best 2,000 compounds to test experimentally.

Out of that came a very striking, potent inhibitor on which we'll be publishing a paper in the next few months. We are now using this same strategy on other proteins. I think it's going to become more and more apparent in the next five to seven years that we really are running out of drug targets. Then, in the 10- to 15-year horizon, some of these new approaches will be successful, and that will lead to some powerful new drugs. It will take some time to get there, though.

—As told to Francie Diep

STAT

20,817

Days in space—the highest of any country—clocked by Russian astronauts as of July 24

14,820 Days in space clocked by Americans on the same date

COURTESY OF BRENT STOCKWELL

COMMENT AT ScientificAmerican.com/oct2011

PHARMACEUTICALS

Clearing the Smoke

Marijuana remains tightly controlled, even though its compounds show promise

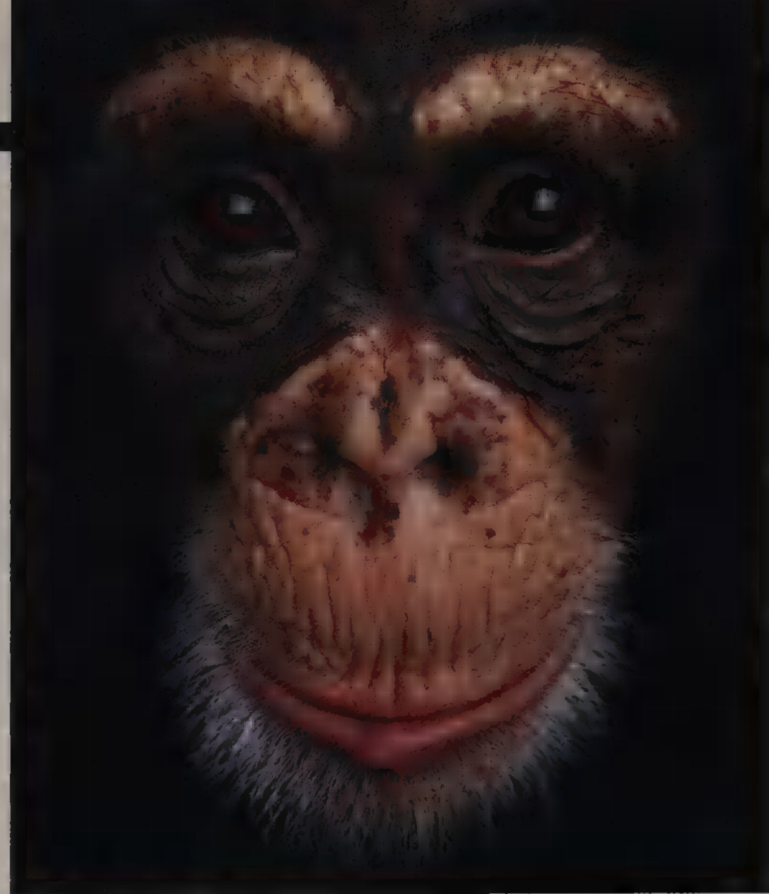
Preliminary clinical trials show marijuana might be useful for pain, nausea and weight loss in cancer and HIV/AIDS and for muscle spasms in multiple sclerosis. Medical marijuana studies in the U.S. are dwindling fast, however, as funding for research in California—the only state to support research on the whole cannabis plant—comes to an end this year and federal regulations on obtaining marijuana for study remain tight.

In July the Drug Enforcement Administration denied a petition, first filed in 2002 and supported by the American Medical Association, to change marijuana's current classification. So marijuana remains in the administration's most tightly controlled category, Schedule I, defined as drugs that "have a high potential for abuse" and "have no currently accepted medical use in treatment in the U.S." Many medical cannabis proponents see a catch-22 in the U.S.'s marijuana control. One of the DEA's reasons for keeping marijuana in Schedule I is that the drug does not have enough clinical trials showing its benefits. Yet the classification may limit research by making marijuana difficult for investigators to obtain.

Even as prospects for whole-plant marijuana research dim, those who study isolated compounds from marijuana—which incorporates more than 400 different types of molecules—have an easier time. The drug's main active chemical, delta 9-tetrahydrocannabinol (THC), is already FDA-approved for nausea and weight loss in cancer and HIV/AIDS patients. The Mayo Clinic is investigating the compound, trade-named Marinol, as a treatment for irritable bowel syndrome. Researchers at Brigham and Women's Hospital in Boston are studying Marinol for chronic pain.

Compared with smoked or vaporized marijuana, isolated cannabis compounds are more likely to reach federal approval, experts say. Pharmaceutical companies are more likely to develop individual compounds because they are easier to standardize and patent. The results should be similar to inhaled marijuana, says Mahmoud ElSohly, a marijuana chemistry researcher at the University of Mississippi, whose lab grows the nation's only research-grade marijuana.

Other investigators say a turn away from whole-plant research would shortchange patients because the many compounds in marijuana work together to produce a better effect than any one compound alone. Inhaling plant material may also provide a faster-acting therapy than taking Marinol by mouth. While ElSohly agrees that other marijuana compounds can enhance THC, he thinks just a few chemicals should re-create most of marijuana's benefits. *—Francie Diep*



EVOLUTION

"I've Got Your Back"

New evidence shows that chimpanzees aren't as selfish as many scientists thought

Charles Darwin had more in common with chimpanzees than even he realized. Before he was universally known for his theory of natural selection, the young naturalist made a decision that has long been hailed as the type of behavior that fundamentally separates humans from other apes.

In 1858, before Darwin published *On the Origin of Species,* his friend Alfred Russel Wallace mailed Darwin his own theory of evolution that closely matched what Darwin had secretly been working on for more than two decades. Instead of racing to publish and ignoring Wallace's work, Darwin included Wallace's outline alongside his own abstract so that the two could be presented jointly before the Linnean Society the following month. "I would far rather burn my whole book than that [Wallace] or any man should think that I had behaved in a paltry spirit," Darwin wrote.

This kind of prosocial behavior, a form of altruism that seeks to benefit others and promote cooperation, has now been found in chimps, the species that Darwin did more than any other human to connect us with. (On page 12, the Science Agenda, about medical testing in chimps, notes other similarities that have been documented in chimps and humans.) In the study, published in the *Proceedings of the National Academy of Sciences USA*, primatologist Frans de Waal and his colleagues at the Yerkes National Primate Research Center at Emory University presented chimps with a simplified version of the choice that Darwin faced.

Pairs of chimps were brought into a testing room where they were separated only by a wire mesh. On one side was a bucket containing 30 tokens that the chimpanzee could give to an experimenter for a food reward. Half of the tokens were of one color that resulted in only the chimpanzee that gave the token receiving a reward. The other tokens were of a different color that resulted in both chimpanzees receiving a food reward. If chimpanzees were motivated only by selfish interests, they would be expected to choose a reward only for themselves (or it should be 50–50 if they were choosing randomly). But individuals were significantly more likely to choose the prosocial outcome compared with the no-partner control.

De Waal says that previous studies showing chimps to be selfish may have been poorly designed. "The chimps had to understand a complex food-delivery system," De Waal wrote via e-mail, "and were often placed so far apart that they may not have realized how their actions benefited others." De Waal added that his study does not rule out the possibility that chimpanzees were influenced by reciprocal exchanges outside the experimental setting such as grooming or social support.

This latter possibility offers exciting research opportunities for the future. Chimpanzee society, like the greater scientific community that studies them, is built around such reciprocal exchanges. Science is a social activity, and sharing the rewards from one another's research allows scientists to improve their work over time. Like the chimpanzees he would bond us with, Darwin recognized the utility of sharing rewards with others. Behaving in a "paltry spirit" was not the proper choice for a cooperative ape.

—Eric Michael Johnson

Adapted from The Primate Diaries, part of Scientific American*'s blog network at http://blogs.ScientificAmerican.com*

NEWS SCAN

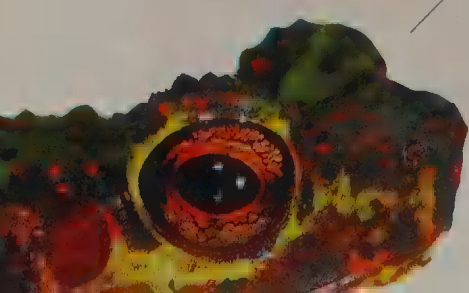
Genius

Earth may have had a second, smaller moon that smacked into the larger one, which explains why one side of the moon is more rugged than the other.

Elephants have social networks ranging from four to 16 "friends." As with people, the smaller the circle, the stronger and more loyal the bond.

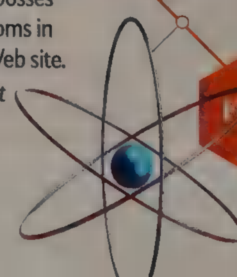
Good news: the wage gap between men and women in science is smaller than in other fields. **Bad news:** women still earn 12 percent less.

Searching remote mountains in Borneo, scientists discover a group of brightly colored rainbow toads, a species last seen in 1924 and believed to be extinct.



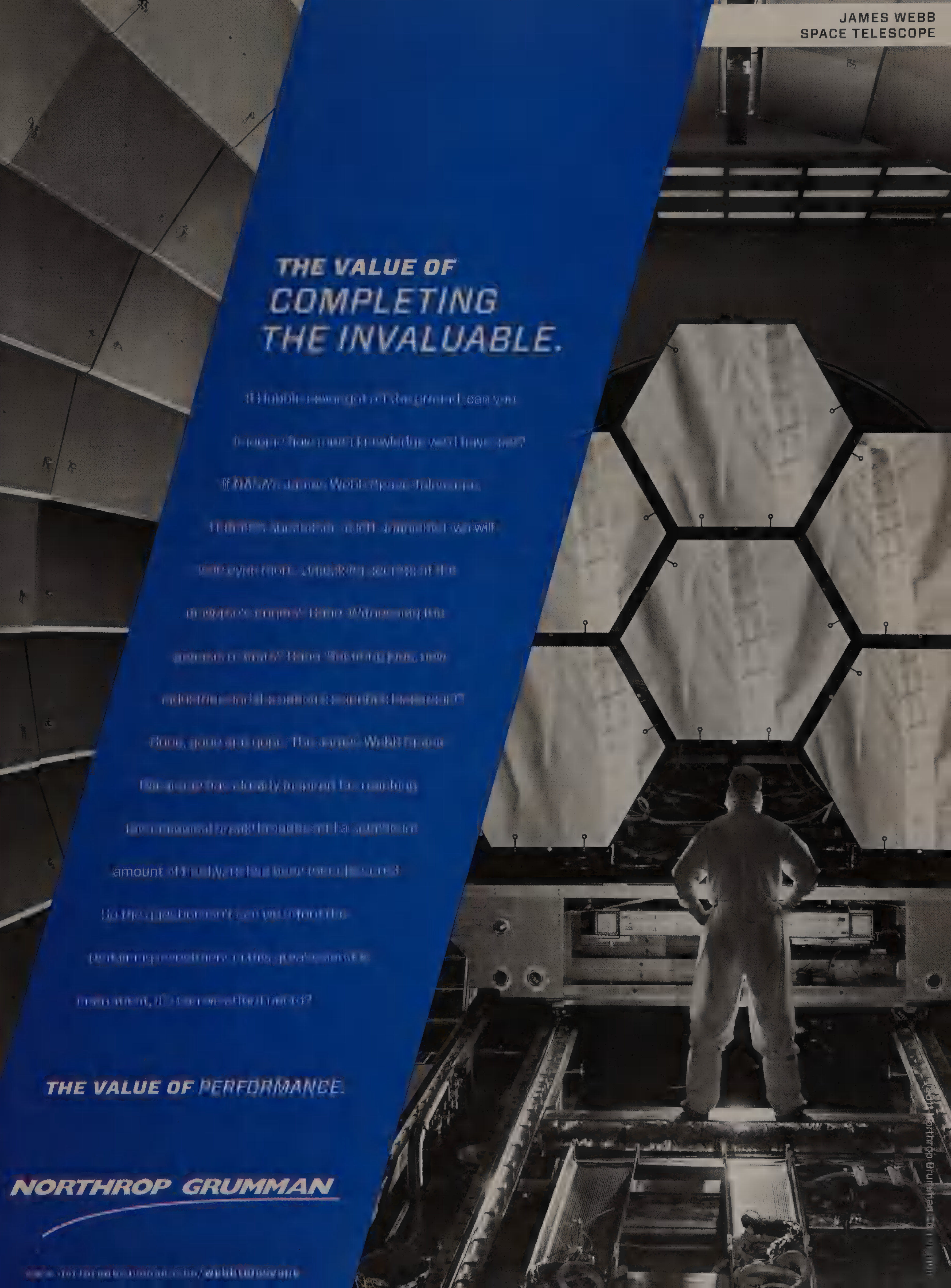
A Swedish man was arrested for unauthorized possession of nuclear materials after trying to split atoms in his kitchen. "It is just a hobby," he wrote on his Web site.

—George Hackett



Folly

BRAD WILSON Getty Images (chimp); AP PHOTO/SEOUL NATIONAL UNIVERSITY (frog); SHAUN LOMBARD Getty Images (elephants); GETTY IMAGES (atom)


JAMES WEBB
SPACE TELESCOPE
THE VALUE OF
COMPLETING
THE INVALUABLE.
THE VALUE OF PERFORMANCE.
NORTHROP GRUMMAN

ENGINEERING

Instant Health Checks for Buildings and Bridges

Sensors can detect damage that may be invisible to the naked eye

YADID LEVY Redux Pictures

During 2011's deadly onslaught of earthquakes, floods and tornadoes, countless buildings had to be evacuated while workers checked to make sure they were stable. The events served as a reminder that most structures are still inspected by a decidedly low-tech method: the naked eye. To speed the process and make it more accurate, investigators are researching electronic skins, evolutionary algorithms and other systems that can monitor the integrity of bridges, buildings, dams and other structures in real time.

To automatically detect tiny faults and relay their precise locations, civil engineer Simon Laflamme of the Massachusetts Institute of Technology and his colleagues are devising a "sensing skin"—flexible patches that glue to areas where cracks are likely to occur and continuously monitor them. The formation of a crack would cause a tiny movement in the concrete under a patch, causing a change in the electrical charge stored in the sensing skin, which is made of stretchable plastic mixed with titanium oxide. Every day a computer attached to a collection of patches would send out a current to measure each patch's charge, a system that Laflamme and his colleagues detail in the *Journal of Materials Chemistry.*

Another engineer is applying a similar concept to bridges. To monitor deterioration inside suspension bridge cables, Raimondo Betti of Columbia University and his collaborators are testing 40 sensors in cables in New York City's Manhattan Bridge (*above*). The sensors track temperature, humidity and corrosion rate.

Although these sensors can detect damage that occurs after they have been installed, what about damage a structure had beforehand? Roboticist Hod Lipson of Cornell University and his colleagues have developed a computer model that simulates an intact structure and runs algorithms that evolve this model until it matches data that sensors provide, which can reveal a broader scope of damage.

Others are not yet convinced of these projects' benefits. "There does not exist, yet, enough research and data that economically support continuous and timely maintenance," Laflamme says. Another concern might be the yet to be studied long-term performance of the systems, especially in harsh environments—a matter for future research.

—Charles Q. Choi

STAT

[494]

Days in space clocked by Japanese astronauts as of July 24, the day Japan surpassed Germany to take third place. (By October 1 Japan will have clocked 563 days thanks to astronaut Satoshi Furukawa's mission onboard the International Space Station)

493 Days in space clocked by German astronauts as of July

COMMENT AT ScientificAmerican.com/oct2011

PHYSIOLOGY

The Trouble with Armor

The steel plates worn by medieval soldiers may have led to their wearers' demise

GETTY IMAGES

On August 13, 1415, the 27-year-old English king Henry V led his army into France. Within two months dysentery had killed perhaps a quarter of his men, while a French army four times its size blocked escape to Calais and across the English Channel. Winter approached; food grew scarce. Yet in one of the most remarkable upsets in military history, a force of fewer than 7,000 English soldiers—most of them lightly armed archers—repulsed 20,000 to 30,000 heavily armored French men-at-arms near the village of Agincourt, killing thousands. Shakespeare's play *Henry V* attributed the victory to the power of Henry's inspirational rhetoric; the renowned military historian John Keegan has credited the self-defeating crush of the French charge. But a study by exercise physiologists now suggests a new reason for the slaughter: suits of armor might not be all that great for fighting.

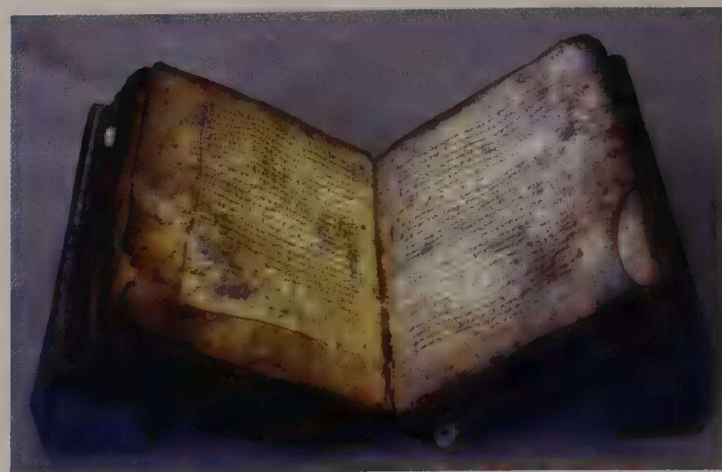
Researchers at the University of Leeds in England placed armor-clad volunteers on a treadmill and monitored their oxygen consumption. The armor commonly used in the 15th century weighed anywhere from 30 to 50 kilograms, spread from head to hand to toe. Because of the distributed mass, volunteers had to summon great effort to swing steel-plated legs through each stride. In addition, breastplates forced quick, shallow breaths. The researchers found that the suits of armor doubled volunteers' metabolic requirements, compared with an increase of only about 70 percent for the same amount of weight carried in a backpack.

Of course, medieval battles did not happen on treadmills. The fields at Agincourt were thick with mud, having recently been plowed for winter wheat and soaked in a heavy October shower. The French charged across 300 yards of this slop, all while suffering fire from the English archers. Combine the effort required to run in armor with that needed to slog through mud, says Graham Askew, one of the study's leaders, and you'd expect at least a fourfold increase in energy expenditure—enough, it seems, to change history. *—Michael Moyer*

HISTORY OF SCIENCE

A Tale of Math Treasure

An exhibition traces the reconstruction of a long-missing collection of writings by Archimedes



Archimedes Palimpsest

There is much cheesy lore about the ancient Greek mathematician Archimedes of Syracuse: that he popularized the word "eureka"; that he used mirrors to set Roman ships on fire; that a Roman soldier killed him in 212 B.C. while he was tracing diagrams in the sand. Not only is the lore probably untrue, historians say, but it also fails to capture the true significance of his achievements, which spanned mathematics, science and engineering and inspired the likes of Leonardo da Vinci, Galileo and Isaac Newton. Some credit him with having essentially invented the basic ideas of calculus.

An exhibit opening in October at the Walters Art Museum in Baltimore will showcase a decade-long effort to restore some of his long-lost texts and unearth some of his previously unknown contributions. "Lost and Found: The Secrets of Archimedes" focuses on a parchment book known as the *Archimedes Palimpsest*.

At one point in history, all of Archimedes' works that survived through the Dark Ages were contained in just three tomes made by 10th-century copyists in Constantinople. One, called *Codex C*, disappeared some time after Western European armies sacked the Byzantine capital in 1204. Then, in 1906, Danish philologist Johan Ludvig Heiberg found a book of prayers at a monastery in the city and noticed that it was a palimpsest—meaning that the parchment had been recycled by cutting up the pages of older books and scraping them clean. Among those older books, Heiberg realized, was *Codex C*. Armed with a magnifying lens, Heiberg painstakingly transcribed what he could read of the older text, including parts of two treatises that no other eyes had seen in modern times. One was the "Method of Mechanical Theorems," which describes the law of the lever and a technique to calculate a body's center of gravity—essentially the one still used today. Another, called the "Stomachion," appeared to be about a tangramlike game. Soon, the book disappeared again before resurfacing in 1998 at an auction in New York City. There an anonymous collector bought it for $2 million and lent it to the Walters museum. When the palimpsest reemerged, says Will Noel, who is its curator, "it was in appalling condition."

As the exhibition will display on panels and videos, imaging experts were able to map much of the hidden text using high-tech tools—including x-rays from a particle accelerator—and to make it available to scholars. Reviel Netz, a historian of mathematics at Stanford University, discovered by reading the "Method of Mechanical Theorems" that Archimedes treated infinity as a number, which constituted something of a philosophical leap. Netz was also the first scholar to do a thorough study of the diagrams, which he says are likely to be faithful reproductions of the author's original drawings and give crucial insights into his thinking. These will be on display, but the studies go on.

Netz is now transcribing the texts contained in the palimpsest, which he estimates at about 50,000 words, most written in a shorthand typical of medieval copyists. He plans to publish a critical edition in the original Greek. "It will take probably several decades to translate it into English," he says.

—Davide Castelvecchi

COURTESY OF ARCHIMEDES PALIMPSEST/JOHN DEAN PHOTOGRAPHY

TECHNOLOGY

Gig.U Is Now in Session

Universities are piloting superfast Internet connections that may finally rival the speed of South Korea's

The U.S. notoriously lags other countries when it comes to Internet speed. One recent report from Web analyst Akamai Technologies puts us in 14th place, far behind front-runner South Korea and also trailing Hong Kong, Japan and Romania, among other countries. The sticking point over faster broadband has been: Who will pay for it? Telecommunications companies have been leery of investing in infrastructure unless they are certain of demand for extra speed. American consumers, for their part, have been content to direct much of their Internet use to e-mail and social networks, which operate perfectly well at normal broadband speeds, and they have not been willing to pay a premium for speedier service.

The exception lies at the seat of learning. Universities and research institutes are always looking for a quicker flow of bits. "We think our researchers will be left behind without gigabit speeds," says Elise Kohn, a former policy adviser for the Federal Communications Commission. Kohn and Blair Levin, who helped to develop the FCC's National Broadband Plan—a congressionally mandated scheme to ensure broadband access to all Americans—are leading a collection of 29 universities spread across the country in piloting a network of one-gigabit-per-second Internet connections. The group, the University Community Next Generation Innovation Project—more commonly referred to as Gig.U—includes Duke University, the University of Chicago, the University of Washington and Arizona State University.

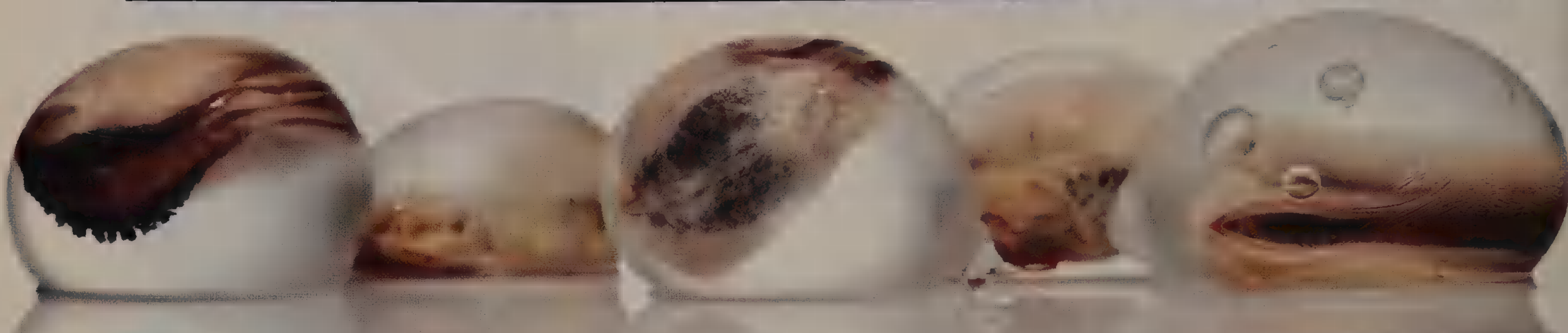
The average U.S. Internet speed today is 5.3 megabits per second, so Gig.U's Internet would be many times faster than those available today, allowing users to download the equivalent of two high-definition movies in less than one minute and to watch streaming video with no pixelation or other interruptions. By comparison, the average Internet speed in South Korea is 14.4 megabits per second, and the country has pledged to connect every home to the Internet at one gigabit per second by 2012.

The U.S. gigabit networks will vary from site to site, depending on the approach that different Internet service providers propose to meet the differing needs of Gig.U members. "All our members are focused on next-generation networks, although some will need more than a gigabit, and others will need less," Kohn says. Gig.U's request-for-information period runs through November to solicit ideas from the local service providers upgrading to faster networks. These ideas will ultimately be funded by Gig.U members, as well as any nonprofits and private-sector companies interested in the project. Gig.U intends to accelerate the deployment of next-generation networks in the U.S. by encouraging researchers—students and professors alike—to develop new applications and services that can make use of ultrafast data-transfer rates. *—Larry Greenemeier*

QUOTABLE

"Some core of the Korean culture has remained intact over at least 1,500 years."

—From a study in the *New Journal of Physics* that found that the most common Korean surname, Kim, has been popular as far back as 500 A.D., when one fifth of the population shared the name.



Adrià's mussels in their juice

FOOD

Spherical Eats

The chemistry of encased mussels and other edible orbs

A few years ago the renowned chef Ferran Adrià presented diners at his restaurant, elBulli, with a simple dish of bright-orange caviar—or rather what looked like caviar: when the guests bit into the orbs, they burst into a mouthful of cantaloupe juice. Since that legendary bit of culinary trompe l'oeil, Adrià and other avant-garde chefs have created many more otherworldly dishes, including mussels that Adrià encases in transparent globes of their own juice.

Eating these spherical foods can evoke childlike joy as you roll the smooth balls around your mouth and explode them with your tongue. But making such confections is not so simple; a lot of chemistry goes into the process.

Chefs have developed two ways to go about it: direct and reverse spherification. Both methods exploit the fact that some gelling mixtures do not set unless ions, charged molecules, are present.

In the direct approach, the chef blends the food into a puree or broth that contains a gelling agent, such as sodium alginate or iota carrageenan, but that lacks coagulating ions. The cook separately prepares a setting bath that contains a source of the missing ions, such as calcium gluconate. As soon as droplets or spoonfuls of the food fall into the bath, gelling begins.

Surface tension pulls the beads into their distinctive round shape. A short dip in the bath yields liquid-filled balls encased in tissue-thin skin; a long soak produces chewy beads. The cook stops the gelling process by rinsing the beads and heating them to 85 degrees Celsius (185 degrees Fahrenheit) for 10 minutes.

Reverse spherification inverts the process: calcium lactate or some other source of calcium ions is added to the edible liquid or puree—unless the food is naturally rich in calcium. The bath contains unset gel made with deionized or distilled water, which is calcium-free. When the food goes in, the bath solution itself forms a skin of gel around it. The culinary team at our lab has used spherification to make marbles of crystal-clear tomato water that enclose smaller spheres of basil oil. We have also found that this technique is a terrific way to make a very convincing-looking raw "egg" out of little more than water, ham broth (for the white) and melon juice (for the yolk). It tastes much better than it looks. *—W. Wayt Gibbs and Nathan Myhrvold*

Myhrvold is author and Gibbs is editor of Modernist Cuisine: The Art and Science of Cooking *(The Cooking Lab, 2011).*

MEDICINE

Putting Diabetes on Autopilot

New devices may spare patients from monitoring their blood glucose

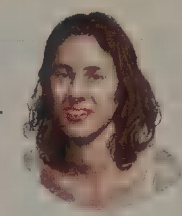
For millions of diabetes sufferers, life is [redacted] constant battle to keep their blood sugar balanced, which typically means they have to test their glucose levels and take insulin throughout the day. A [redacted] generation of "artificial pancreas" devices may make tedious diabetes micromanagement obsolete. In healthy people, the pancreas naturally produces insulin, which converts sugars and starches into energy. People with type 1 diabetes, however, do not produce any insulin of their own, and those with type 2 produce too little. All type 1 and many type 2 diabetics have to dose themselves with insulin to keep their bodies fueled—and doing so properly requires constant monitoring of blood sugar because appropriate dosages depend on factors such as how much patients eat or exercise. Stuart Weinzimer, an endocrinologist at Yale University, has devised an artificial pancreas that combines two existing technologies: a continuous glucose monitor, which uses an under-the-skin sensor to measure blood glucose levels every few minutes, and an insulin pump, which dispenses insulin through a tube that is also implanted under the skin. The glucose [redacted] sends its data wirelessly to [redacted] pocket computer a little bigger than an iPhone that is loaded with software developed by Minneapolis-based Medtronic. The program scans the incoming data from the glucose monitor and directs the pump to dispense the correct amount of insulin.

At an American Diabetes Association meeting in June, Weinzimer and his colleagues reported that [redacted] percent of type 1 diabetics they studied who used the artificial pancreas reached target blood glucose levels at night, whereas only 54 percent of subjects who had to wake up to activate an insulin pump reached their target levels. Other, similar systems are in development at Boston University, the University of Cambridge and Stanford University.

Some technical glitches still need to be worked out. For example, the device occasionally has trouble adapting to drastic changes in glucose, such as those that occur after exercise. And it will have to go through more rounds of vetting, which could take years, including large-scale patient trials that will be required before the Food and Drug Administration can approve the device. Nevertheless, Weinzimer says that the enthusiastic responses he has gotten from his trial participants remind him why the long slog toward commercialization is worthwhile. *—Elizabeth Svoboda*

RYAN MATTHEW SMITH *Modernist Cuisine LLC*

COMMENT AT ScientificAmerican.com/oct2011



Laura Blue is a Ph.D. student in demography at Princeton University.

The Ethnic Health Advantage

Two populations in the U.S. tend to outlive their often richer neighbors. Why?

For decades scholars and public health officials have known that people with greater income or formal education tend to live longer and enjoy better health than their counterparts who have less money or schooling. The trend holds true wherever researchers look—in poor countries or rich ones, in Europe, Asia or the Americas—but two notable exceptions stand out.

One is known as the healthy immigrant effect. Looked at as a group, immigrants to countries as diverse as the U.S., Australia, Germany and Canada live longer than their new native-born neighbors. Yet immigrants also tend to be less well educated and are often more likely to live in poverty in those countries.

The other exception is called the Hispanic paradox and is particular to the U.S. In study after study, people of Hispanic descent (typically of Spanish, Mexican, Cuban, Puerto Rican, or Central or South American origin) seem to live longer than non-Hispanic whites, who on average happen to be richer and better educated. In 2006, for example, life expectancy at birth in the U.S. was 2.5 years higher for Hispanics than for non-Hispanic whites. The paradox is real; data errors, such as small sample size or the underreporting of Hispanic ethnicity on death certificates, cannot explain it. Yet the cause of the paradox has long been a mystery.

Recently I took a closer look at both the healthy immigrant effect and the Hispanic paradox with Andrew Fenelon, a graduate student at the University of Pennsylvania. Fenelon studies sociology and, like me, demography—a relatively small field that I often describe as the ecology of human populations. Just like ecologists, demographers are interested in the fertility, mortality and migration patterns of certain species; in our case, that species is humans. Samuel Preston, one of the world's leading demographers (and Fenelon's Ph.D. adviser), had a hunch about what might cause the U.S. Hispanics' longevity advantage in particular, and Fenelon and I had some ideas about how to test that hunch and to see if it applied as well to the immigrant advantage.

Today Fenelon and I believe we can largely explain both anomalies. If our research is correct, then it largely stems from just one factor—a factor that was hiding in plain sight all along.

UNRAVELING A MYSTERY

Scholars have come up with many hypotheses to explain the general immigrant advantage, and most of these ideas simultaneously attempt to account for the more specific Hispanic paradox as well. They link the two phenomena because many Hispanics in the U.S. are immigrants: according to the latest census data, two out of five Hispanics living in the U.S. were not born there.

Among the most popular explanations for the immigrant advantage is that such individuals might be unusually resilient, both mentally and physically. They must, after all, need energy and motivation to leave their homes and build a new life on foreign soil, the thinking goes. At the very least they are not likely to be on their deathbeds when they move. Perhaps, therefore, immigrants are simply healthier than the average person when they arrive in the U.S. Alternatively, maybe immigrants who get sick leave the U.S. and return home for care, which would then leave the population of remaining immigrants unusually healthy.

In addition to a putative immigrant advantage, proposed explanations for the Hispanic paradox generally emphasize culture and lifestyle. Hispanics in the U.S. could have stronger family ties that may help steer them through periods of ill health and stress. Another possibility: Hispanics might eat more nutritious foods. Or their work and leisure activities might be more physically demanding, which promotes physical fitness. All these notions are plausible. Yet to date, no studies have been convincingly able to link such behaviors to the Hispanic lifespan advantage.

One lifestyle factor, however, correlates with elevated death rates in almost every mortality study of any population in the world: smoking.

Illustration by Edel Rodriguez

Bakuriani, Georgia

Could something as obvious as smoking explain immigrants' and Hispanics' life expectancy advantage in the U.S.? This is the theory that Fenelon and I set out to test. In 2009 and 2010 we conducted two analyses of National Vital Statistics System and Census Bureau data from 2000: one to compare Hispanics with non-Hispanic whites (with no regard to birthplace) and a second to compare immigrants with native-born Americans (with no regard to ethnicity). Regrettably, we could not specifically compare immigrant and native Hispanics; there are not enough data about older U.S.-born Hispanics to generate statistically valid estimates of total life expectancy for the purposes of comparison. In each analysis, we estimated the number of deaths attributable to smoking for each group we were comparing and then checked how much of the difference in total death rates could be explained by smoking. We used death from lung cancer as a marker for smoking-related death because lung cancer is the condition most strongly tied to smoking. We then used death from lung cancer to extrapolate death from all smoking-related conditions.

The strength of the results, published this year in the *International Journal of Epidemiology,* surprised even us. We found that smoking is the single best explanation of the Hispanic paradox and the general immigrant advantage, at least among adults. Our results show that in 2000 smoking explained more than 75 percent of the difference in life expectancy at age 50 between Hispanic and non-Hispanic white men and roughly 75 percent among women. It also accounted for more than 50 percent of the difference in life expectancy at age 50 between foreign- and native-born men and more than 70 percent of the difference among women. We cannot know from these estimates whether less smoking means that foreign-born Hispanics live longer than their U.S.-born Hispanic counterparts, because we did not estimate death rates separately for these groups. But recent data are not inconsistent with that idea: Fenelon has found that foreign-born Hispanics do smoke substantially less than U.S.-born Hispanics do.

HIDING IN PLAIN SIGHT: A single, overlooked factor may well solve two demographic mysteries at once.

People ask me how it is that no one noticed the role of smoking before. Of course, people did know that smoking is bad for health. But the extent of its role in health disparities between ethnic groups was not much recognized, perhaps because most studies of health habits in different populations have been based on large-scale surveys, which typically do not include tremendous detail about smoking and thus do not reveal differences in smoking habits between groups.

Consider, for example, a typical health survey, which somewhat resembles the health history form you often fill out when you visit a new doctor. The form will probably ask whether you smoke now and whether you used to smoke. But smokers and former smokers are rarely asked precisely how long they smoked and how many cigarettes a day they consumed at every point in their lives. Even if the questions were asked, people might misremember exactly how much they smoked several decades ago.

Nevertheless, a number of studies based on survey data have picked up some ethnic differences in smoking prevalence (whether or not people smoke)—and this was exactly the kind of information that inspired Fenelon and me to determine whether smoking was the key factor in the Hispanic paradox. But those surveys have generally failed to notice ethnic differences in smoking intensity and duration or how much smokers are smoking. At least one set of data, however, does address such details. The National Health Interview Survey, an annual questionnaire that asks fairly detailed questions about tobacco use, has shown that Hispanics are not only less likely to be smokers or former smokers but that the smokers among them are also less likely to smoke heavily. In 2009, for instance, only 9 percent of Hispanic women were current smokers, compared with 21 percent of non-Hispanic white women; 18 percent of Hispanic men smoked, compared with 25 percent of non-Hispanic white men. Among smokers, Hispanics also consumed far fewer cigarettes on average.

When I say that the answer to the immigrant and Hispanic paradoxes may have been "hiding in plain sight all along," I am referring to the kind of information in the national health survey. In the case of Hispanics in the U.S., scholars recognized that smoking prevalence was unusually low among that group, and the data were there to check whether smoking intensity was low as well. But no one took the next step of calculating whether differences in total cigarette consumption could be so large as to drive the overall life expectancy advantage among Hispanics. My research with Fenelon has done that.

We estimated smoking-attributable deaths not from survey data but instead from aggregate national death data: records of every single death in the U.S. in 2000. These data have plenty of their own drawbacks, to be sure. Crucially, our methods depend on the assumption that records of deaths from lung cancer are equally reliable in all subpopulations. To limit the impact of our assumptions on our final results, Fenelon and I used a few different methods to estimate smoking-attributable deaths, and the methods all yielded similar answers. We also took into account the possibility that immigrants may return to their home countries to die. We still found that, yes, smoking makes the difference in longevity.

I cannot say why Hispanics historically have smoked less than non-Hispanic whites. What is clear, however, is that millions of Americans have turned away from smoking since its health effects became obvious in the second half of the 20th century. Meanwhile cigarette consumption is on the rise in much of the developing world, thanks in no small part to strong marketing from tobacco companies. Together these two trends suggest that, over time, immigrants' life expectancy advantage in the U.S. may erode. I expect that both the immigrant advantage and the Hispanic paradox may disappear within the next few decades.

No one who reads this article will be surprised to learn that smoking kills. But sometimes we forget how profound its effects on health can be. In the case of Hispanics in the U.S., low cigarette consumption seems powerful enough to counteract a slew of socioeconomic disadvantages that often result in poor health and early death. That is a finding worth remembering for everyone.

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/oct2011

David Pogue is the personal-technology columnist for the *New York Times* and an Emmy Award–winning correspondent for *CBS News.*

Big Progress on the Little Things

Let's take a step back and praise three unsung trends in consumer electronics

In the trenches of consumer technology, there's plenty to complain about. Today's cell-phone contracts are exorbitant and illogical (why has the price of a text message doubled in three years?). Those 15-second voicemail instructions still seem to last forever and use up our expensive airtime ("When you have finished recording, you may hang up"—oh, really?). And laptop batteries still can't last the whole day.

But here and there, in unsung but important corners of consumer tech, some long-standing annoyances have quietly been extinguished. These developments deserve a lot more praise than they've received.

Take the megapixel race. For years the camera industry brainwashed us into believing that a camera's megapixel measurement somehow indicates the quality of its photographs.

It doesn't. A lousy photo still looks lousy—even at 45 megapixels. In fact, more megapixels can mean *worse* images because the more photo sites (light-sensing pixels) you cram onto a sensor, the smaller they get, the less light they collect and the more heat they produce, resulting in "noise" (random speckles).

The megapixel myth was a convenient psychological cop-out for consumers, who longed for a single, comparative statistic like miles per gallon for a car or gigabytes for an iPod. The camera companies played right along because it meant that they didn't have to work on the factors that really do produce better pictures: the lens, the software and, above all, the sensor size.

In the past two years, though, a quiet revolution has taken place. The megapixel race essentially shut itself down. The megapixel count came to rest at 10 or 12 megapixels for pocket camer-

as, maybe 16 or 18 for professional ones—and the camera companies began putting their development efforts into bigger sensors. Cameras such as the Canon S95, the Sony NEX-C3 and Micro Four Thirds models pack larger sensors into smaller bodies.

Another example: power cords. We've all griped at one time or another about our drawers full of ugly, mutually incompatible chargers. Every new cell-phone model, even from the same manufacturer, used to require a different cord (and car and plane adapters), racking up another $50 per phone sale per customer.

And then, one great morning, electronics executives must have confronted themselves in the mirror, filled with shame, and decided to shut down that extortionist, environmentally disastrous profit center.

In Europe, for example, all the major cell-phone makers agreed to standardize their cords. Today every phone model uses exactly the same interchangeable micro USB power cord.

Similarly, the micro USB's cousin, the mini USB, has been making its own conquests. Now you can charge up most BlackBerries, Bluetooth headsets, e-book readers, music players and GPS receivers by connecting a USB cable to either a power plug or your laptop. You can also use the same 30-pin charging cord on every one of the 200 million iPhones, iPads and iPod touches ever made.

Finally, it's time to give thanks for the most important revolution of all: the simplicity movement.

SCIENTIFIC AMERICAN ONLINE
Read about the tech world's four worst trends at ScientificAmerican.com/oct2011/pogue

IT'S TIME TO GIVE THANKS
for the most important revolution of all: the simplicity movement.

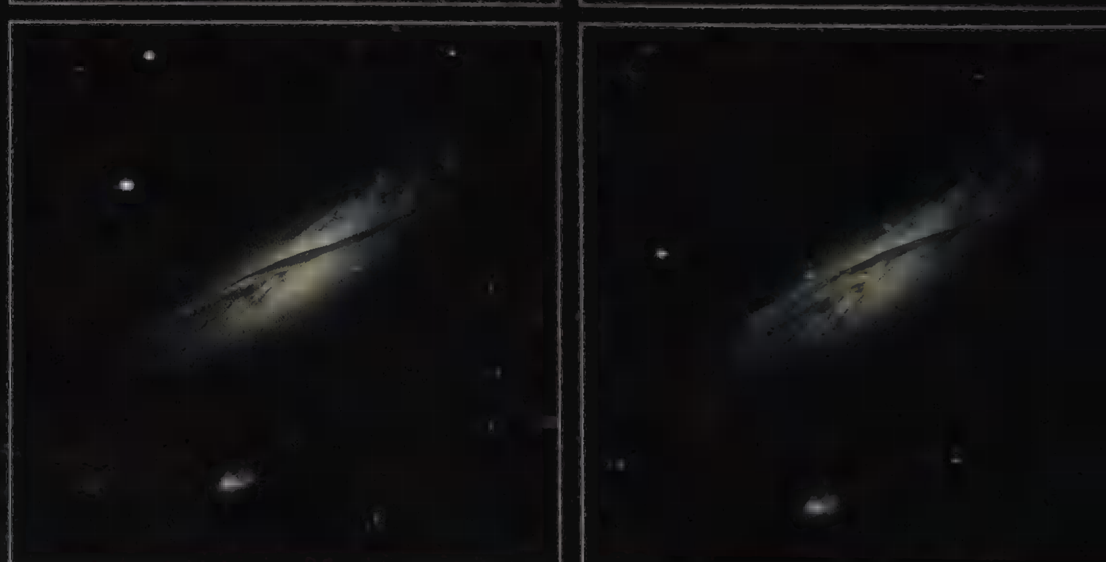
For decades the rule in consumer tech was that whoever packs in more features wins. Our gadgets quickly became complex, cluttered and intimidating.

But then came the iPod, a music player with *fewer* features than its rivals (no radio, no voice recorder); it became the 800-pound gorilla of music players. Then the Flip camcorder—so simple, it didn't even have a zoom—snapped up 40 percent of the camcorder market (until Cisco bought and, inexplicably, killed it). And the Wii, a game console whose controller has half as many buttons as the Xbox's or the PlayStation's and whose graphics look Fisher-Price crude, became a towering success, outselling its rivals year after year.

Simplicity works because it brings you happiness. You feel a sense of immediate mastery. Simplicity as a design goal makes life harder for the gadget makers, of course, because designing next year's model is no longer as easy as piling on new features. But simplicity is a goal worth sweating for.

In other words, some trends demonstrate maturity, brains and good taste on the part of the manufacturers; it's worth taking a moment to celebrate them.

Okay, that's enough. Now let's go back to complaining. SA



[illegible] The disk of the Milky Way has developed a warp, which astronomers think is not a static distortion but a slow-motion wave, like the vibration of a gong or drumhead. The author argues that the vibration is set in motion by disturbances in the galaxy's dark matter, which in turn are triggered by two small satellite galaxies.

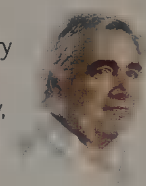
ASTROPHYSICS

THE DARK SIDE OF THE MILKY WAY

Dark matter is not just a puzzle. It is a solution

By Leo Blitz

Leo Blitz wanted to be an astronomer since early elementary school, when his favorite TV show was *Watch Mr. Wizard*. He is now a professor at the University of California, Berkeley, and is former director of the Radio Astronomy Laboratory.



ALTHOUGH ASTRONOMERS ONLY SLOWLY CAME TO REALIZE dark matter's importance in the universe, for me personally it happened in an instant. In my first project as a postdoc at the University of California, Berkeley, in 1978, I measured the rotational velocities of star-forming giant molecular clouds in the outer part of the disk of our Milky Way galaxy. I worked out what was then the most accurate method to determine those velocities, and I sat down to plot out the results (by hand on graph paper) in the astronomy department lounge. Two other experts on the Milky Way, Frank Shu and Ivan King, happened by. They watched as I filled in the velocities of the outermost clouds, and the pattern we saw made it clear at once that the Milky Way was rife with dark matter, especially in its outermost parts. We sat and scratched our heads, imagining what the nature of the dark matter could be, and all the ideas we came up with turned out in short order to be wrong.

This study was one of many in the 1970s and 1980s that forced astronomers to conclude that dark matter—a mysterious substance that neither emits nor absorbs light and reveals itself solely by its gravitational influence—not only exists but is the dominant material constituent of the universe. Measurements with the WMAP spacecraft confirm that dark matter accounts for five times as much mass as ordinary matter (protons, neutrons, electrons, and so on). What the stuff is remains as elusive as ever. It is a measure of our ignorance that the most conservative hypothesis proposes that dark matter consists of an exotic particle not yet detected in particle accelerators, predicted by theories of matter that have not yet been verified. The most radical hypothesis is that Newton's law of gravity and Einstein's general theory of relativity are wrong or, at the very least, require unpleasant modifications.

Whatever its nature, dark matter is already providing keys to unlock some persistent puzzles about how the Milky Way came to have certain of its features. For example, astronomers have known for more than 50 years that the outer parts of the galaxy are warped like a vinyl phonograph record left on a heater. They could not make a viable model for the warp—until they considered the effects of dark matter. Similarly, computer simulations of galactic formation based on the assumed properties of dark matter predicted that our galaxy should be surrounded by hundreds or even thousands of small satellite galaxies. Yet observers saw only about two dozen. The discrepancy led people to question whether dark matter had the properties they thought it did. But in recent years several groups of astronomers have discovered troves of dwarf satellites, narrowing the disparity. These newly located satellites are not only helping to

IN BRIEF

Dark matter is one of the great scientific mysteries of our time, but once astronomers accepted its existence, the answers to many other cosmic mysteries fell into place.

Whatever this unknown material may be, it seems to explain why the disk of our Milky Way galaxy has such a pronounced warp at its outer rim. Orbiting satellite galaxies naturally tend to distort the galaxy, but their gravitational effect would be too weak without the amplification that dark matter provides.

Another question dark matter answers is why the Milky Way appears to have fewer such satellite galaxies than models predict it should. It turns out that the satellites are probably out there, though composed almost entirely of dark matter, making them hard to detect.

Large Magellanic Cloud, the biggest satellite galaxy of the Milky Way, may be stirring up our galaxy's dark matter.

COURTESY OF ECKHARD SLAWIK

resolve a long-standing mystery of galactic structure; they may also be teaching us something about the total cosmic inventory of matter.

FACTORING IN THE WARP

A FIRST STEP to understanding what dark matter tells us about the Milky Way is to get a general picture of how the galaxy is organized. Ordinary matter—the stars and gas—resides in four major structures: a thin disk (which includes the pinwheel-like spiral pattern and the location of the sun), a dense nucleus (which also harbors a supermassive black hole), an elongated bulge known as the bar, and a spheroidal "halo" of old stars and clusters that envelops the rest of the galaxy. Dark matter has a very different arrangement. Although we cannot see it, we infer where it is from the rotation velocities of stars and gas; its gravitational effects on visible material suggest it is approximately spherically distributed and extends far beyond the stellar halo, with a density that is highest at the center and falls off approximately as the square of the distance from the center. Such a distribution would be the natural result of what astronomers call hierarchical merging: the proposition that in the early universe, smaller galaxies accreted to build larger ones, including the Milky Way.

For years astronomers could get no further than this basic picture of dark matter as a giant, undifferentiated ball of unidentified material. In the past several years, however, we have managed to glean more details, and dark matter has proved rather more interesting than we had suspected. Various lines of evidence suggest that this material is not smoothly distributed but has some large-scale lumpiness to it.

Such unevenness would explain the existence and size of the galactic warp. When astronomers say the galaxy is warped, we are referring to a specific distortion in the outskirts of the disk. At distances beyond about 50,000 light-years from the center, the disk consists almost entirely of atomic hydrogen gas, with only a few stars. Mapped by radio telescopes, the gas does not lie in the plane of the galaxy; the farther out you go, the more it deviates. By a distance of about 75,000 light-years, the disk has bent about 7,500 light-years out of the plane [*see box on next page*].

Evidently, as the gas within the disk revolves around the galactic center, it also oscillates up and down, in and out of the plane. These oscillations occur over hundreds of millions of years, and we catch them at one moment in their cycle. In essence, the gas disk acts as a kind of giant gong vibrating in slow motion. Like a gong, it can vibrate at multiple frequencies, each corresponding to a certain shape of the surface. In 2005 my colleagues and I showed that the observed warp is the sum of three such frequencies. (The lowest is 64 octaves below middle C.) The overall effect is asymmetric: gas on one side of the galaxy is much farther from the plane than gas on the other side.

The radio astronomers who first noticed the warping in the

Galactic Warp Factor

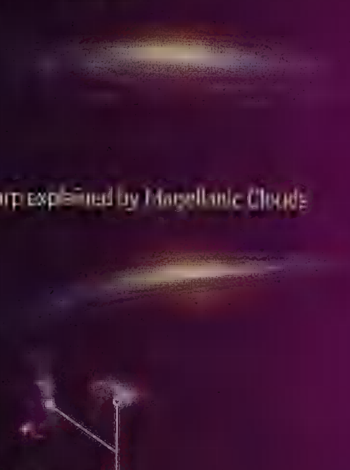
The disk of our Milky Way galaxy, which contains most of its stars and gas, has roughly the proportions of a vinyl LP record or compact disk. The warp in the galaxy looks like what happens when you mistreat an LP or CD.

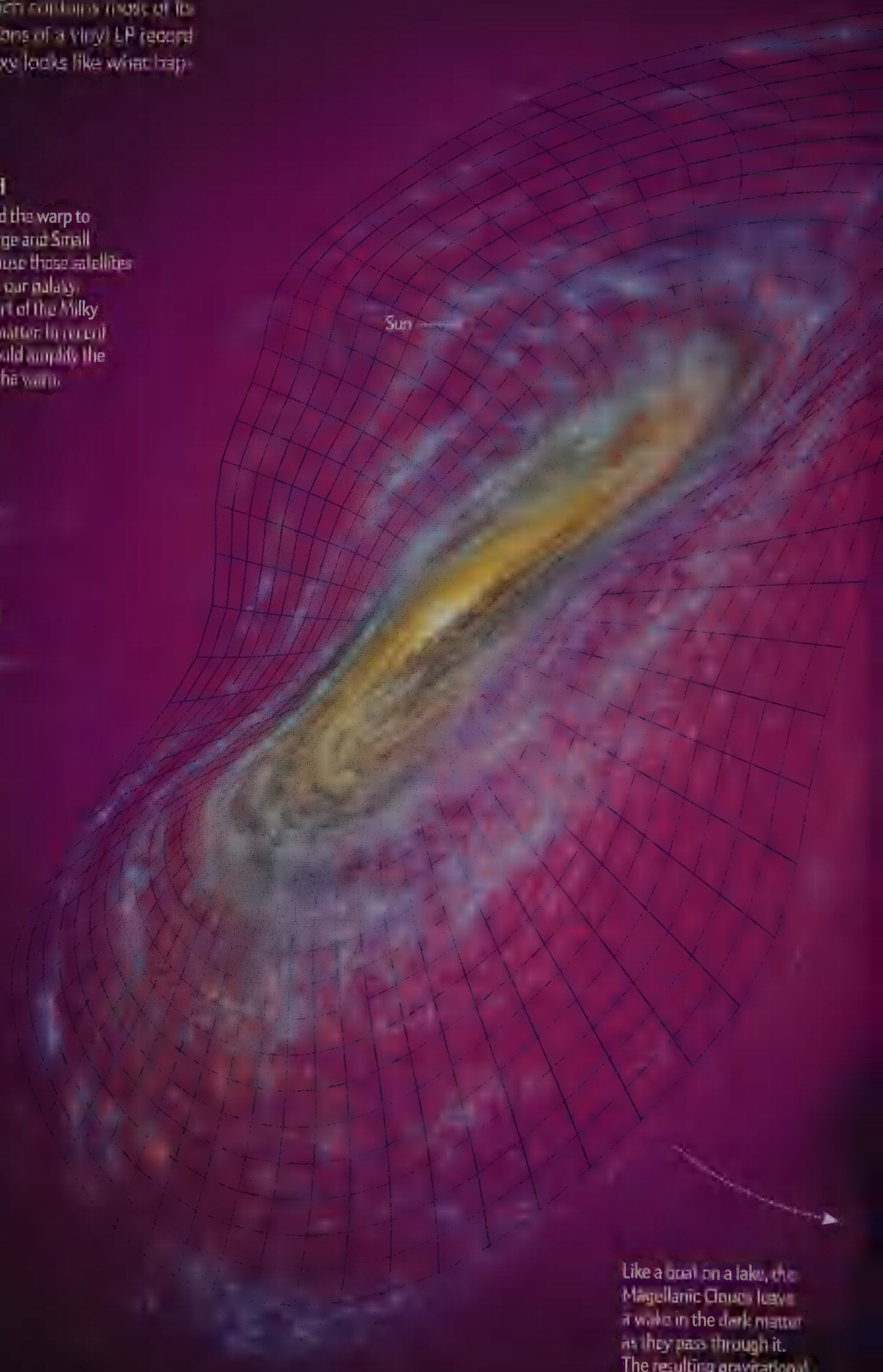
An Old Hypothesis Revisited

A hypothesis dating to the 1950s attributed the warp to the gravity of two satellite galaxies, the Large and Small Magellanic Clouds. It fell into disfavor because those satellites are too lightweight to have much effect on our galaxy. Astronomers now know that the visible part of the Milky Way is surrounded by a huge ball of dark matter. In recent years they have shown that dark matter could amplify the clouds' gravitational influence, explaining the warp.

Classic view of Milky Way

Some warp explained by Magellanic Clouds





Like a boat on a lake, the Magellanic Clouds leave a wake in the dark matter as they pass through it. The resulting gravitational disturbance creates the observed warp.

Vertical scale exaggerated

1950s thought it might result from gravitational forces exerted by the Magellanic Clouds, the most massive galaxies in orbit around the Milky Way. Because these satellite galaxies are orbiting out of the plane of the Milky Way, their gravity tends to distort the disk. Detailed calculations, however, showed that these forces are too weak to explain the effect because the Magellanic Clouds are puny in comparison to the Milky Way. For decades the reason for the pronounced warp remained an unsolved problem.

Vibrating Like a Giant Gong

The warp represents a wave motion captured at one moment in time. The wave has three distinct components corresponding to three natural frequencies of the disk—as though the galaxy were a giant gong. The gravity of the Magellanic Clouds, aided by dark matter, acts as the hammer.

SOURCE: GYULA JÓZSA (*warp shape insets*)

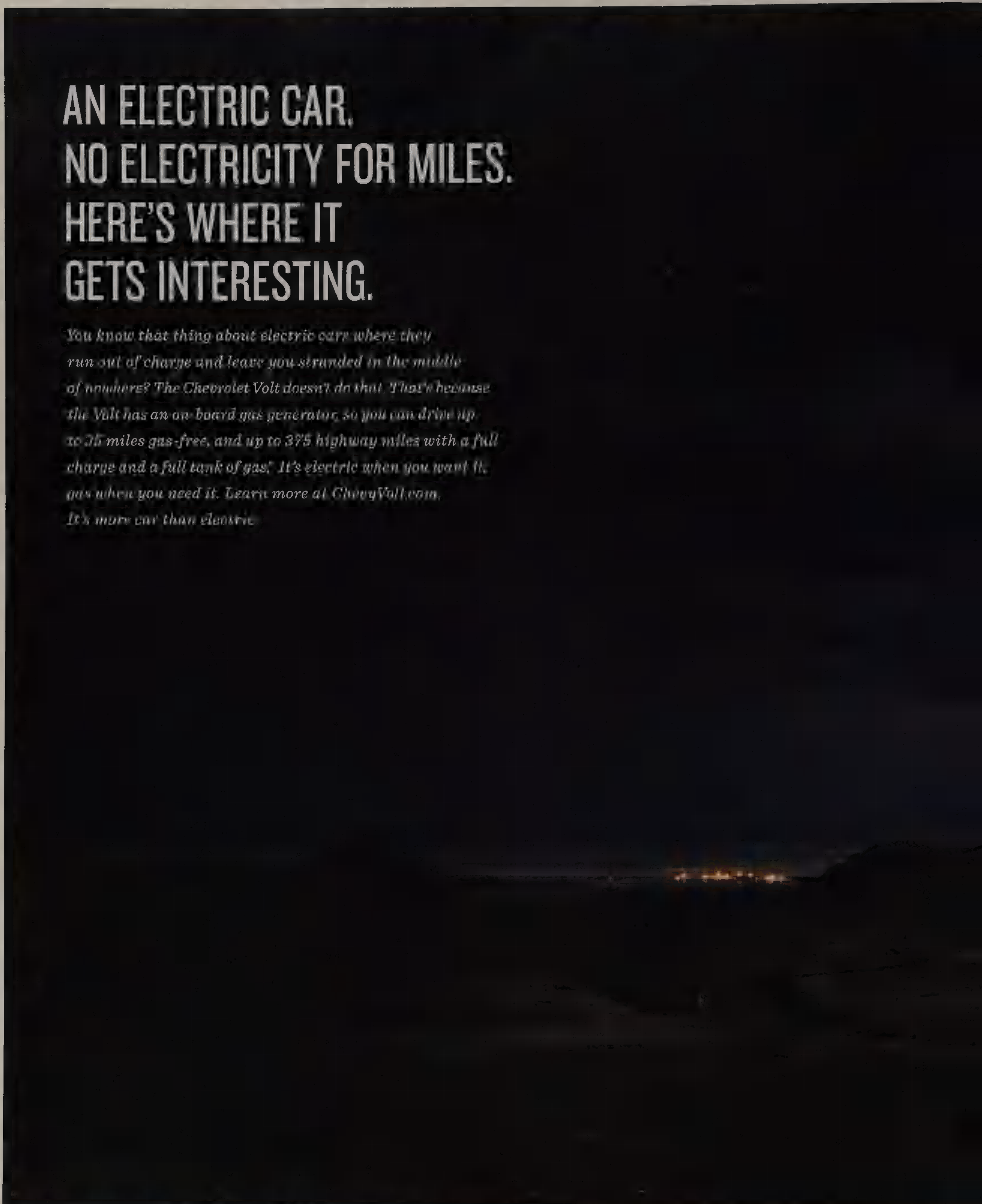
DARK HAMMER

THE RECOGNITION that the Milky Way contains dark matter, together with new estimates of the mass of the Magellanic Clouds (which showed them to be more massive than thought), raised a new possibility. If the gas disk acts as a giant gong, the orbit of the Magellanic Clouds through the dark matter halo can act as a hammer ringing the gong, sounding its natural notes or resonant frequencies, albeit not directly. The clouds create a wake in the dark matter, just as a boat forms a wake as it plows through the water. In this way, the clouds create some unevenness in the distribution of dark matter. That, in turn, acts as the hammer to cause a ringing in the low-mass, outer parts of the disk. The upshot is that even though the Magellanic Clouds are puny, dark matter greatly amplifies their effects.

Martin D. Weinberg of the University of Massachusetts Amherst put forward this general idea in 1998. He and I later applied it to observations of the Milky Way and found we could reproduce the three vibration patterns of the gas disk. If the theory is correct, the warp is an active feature of the Milky Way with a shape that continually changes as the Magellanic Clouds move through their orbits. The shape of the galaxy is not fixed but ever shifting. [*Editors' note: A video of this process is available at www.ScientificAmerican.com/oct2011/blitz.*]

The warp is not the only asymmetry in the shape of the Milky Way. One of the most striking is the lopsided thickness of the outer gas disk, also discovered using radio telescopes. If one drew a line from the sun to the center of the Milky Way and extended it outward, one would find that the thickness of the gas layer on one side of this line is, on average, about twice that on the other side. This large asymmetry is dynamically unstable and, left to its own devices, would tend to right itself; its persistence requires some sort of mechanism to maintain it. For 30 years astronomers knew about the problem but swept it under the rug. They revisited it only very recently when a much improved new survey of the Milky Way's atomic hydrogen, coupled with a better understanding of the noncircular motions of the gas, made the asymmetry impossible to ignore any longer.

The two leading explanations both involve dark matter. Either the Milky Way is spherical but not concentric with its dark matter halo, or as Kanak Saha of the Max Planck Institute for Extraterrestrial Physics in Garching and several collaborators recently argued, the dark matter halo is itself somewhat asymmetric. Both call into question astronomers' old view that the Milky Way and the halo formed together from the condensation of a single gargantuan cloud of material; if it had, the ordinary matter and the dark matter should be centered on the same point. Therefore, the asymmetry is further evidence the galaxy formed from the merging of smaller units or grew by


AN ELECTRIC CAR.
NO ELECTRICITY FOR MILES.
HERE'S WHERE IT
GETS INTERESTING.
You know that thing about electric cars where they run out of charge and leave you stranded in the middle of nowhere? The Chevrolet Volt doesn't do that. That's because the Volt has an on-board gas generator, so you can drive up to 35 miles gas-free, and up to 375 highway miles with a full charge and a full tank of gas.* It's electric when you want it, gas when you need it. Learn more at ChevyVolt.com.
It's more car than electric.

continued merging or accretion of intergalactic gas—processes that need not be symmetric. The center of the galaxy could be offset from the center of the dark matter because gas, stars and dark matter behave differently.

A way to cross-check this idea is to study the long, thin streams of stars that stretch through the outer reaches of the galaxy. These formations are the elongated remains of former satellite galaxies. The most common kind of galaxy to be found in orbit about the Milky Way system is known as a dwarf spheroidal because of its roundish shape and small mass of stars—typically only about one ten-thousandth that of the Milky Way. Over time its orbit decays, and the satellite becomes subject to the tidal forces of the Milky Way. These forces are the same as those produced by the moon on Earth, stretching out the mass of water on Earth as our planet rotates, producing the twice-daily ocean tides. The dwarf galaxy gets stretched out and can be reduced to a thin ribbon [see "The Ghosts of Galaxies Past," by Rodrigo Ibata and Brad Gibson; SCIENTIFIC AMERICAN, April 2007].

Because the stars in these streams orbit the galaxy at large distances, where the gravitational effects of dark matter are large, the shapes of the streams probe the shape of the halo. If the halo is not perfectly spherical but somewhat flattened, it will exert a torque on the orbits of stars in the stream and cause a marked deviation from a great circle. As it happens, the streams are observed to be very thin, and their orbits around the galaxy are nearly great circles. Computer simulations by Ibata and his colleagues therefore suggest that the dark matter distribution is close to spherical, although it might nonetheless be as lopsided as suggested by Saha and his colleagues.

GALAXIES GONE MISSING

IF THE DESTRUCTION of dwarf galaxies raises questions, so does their formation. In our current models, galaxies begin as agglomerations of dark matter, which then accrete gas and stars to form their visible parts. The process yields not only large galaxies such as ours but also numerous dwarfs. The models get the properties of these dwarfs about right but predict far more of them than observers see. Does the fault lie in the models or with the observations?

Part of the answer comes from new analyses of the Sloan Digital Sky Survey, a systematic scan of about a quarter of the sky. The survey has turned up about a dozen new, extremely dim galaxies in orbit around the Milky Way. Their discovery is astonishing. The sky has been so completely surveyed for so long that it is difficult to imagine how galaxies on our cosmic doorstep could have lain undiscovered all this time. These galaxies, known as ultrafaint dwarfs, in some cases contain only a few hundred stars. They are so feeble and diffuse that they do not show up on ordinary images of the sky; it requires special data-handling techniques to identify them.

Had the Sloan survey covered the entire sky when the ultrafaint galaxies were discovered, it might have discovered another 35 or so more. Still, that would not account for all the "missing" dwarfs. So astronomers have sought other possibilities. Perhaps more such galaxies are out there, too far away for existing telescopes to detect. The Sloan survey can find ultrafaint dwarfs out to a distance of about 150,000 light-years. Erik Tollerud and his collaborators at the University of California, Irvine, predict that as many as 500 undiscovered galaxies orbit the Milky Way at distances up to around one million light-years from the center. Astronomers should be able to find them with a new optical telescope called the Large Synoptic Survey Telescope, which will have eight times the collecting area of the Sloan telescope. Construction began on the observatory this past March.

Another hypothesis is that the Milky Way is orbited by galaxies even dimmer than the faintest ultrafaint dwarfs—so dim, perhaps, that they contain no stars at all. They are almost pure dark matter. Whether such galaxies could ever be seen depends on whether they contain gas in addition to the dark matter. Such gas might be sufficiently diffuse that it cools only very slowly, too slowly to have formed stars. Radio telescopes surveying large patches of the sky might nonetheless detect the gas.

If these galaxies lack gas, however, they would reveal their presence only indirectly, by their gravitational effects on ordinary matter. If one of these dark galaxies hurtled through the disk of the Milky Way or some other galaxy, it might leave a splash like that of a pebble thrown into a quiet lake—observable as perturbations to the distribution or velocities of stars and gas. Unfortunately, this splash would be very small, and astronomers would have to convince themselves that it could not be made in any other way—a daunting task. All spiral galaxies show disturbances throughout their atomic hydrogen disks akin to waves in a rough sea.

A small galaxy consisting purely of dark matter may now be hurtling through the Milky Way.

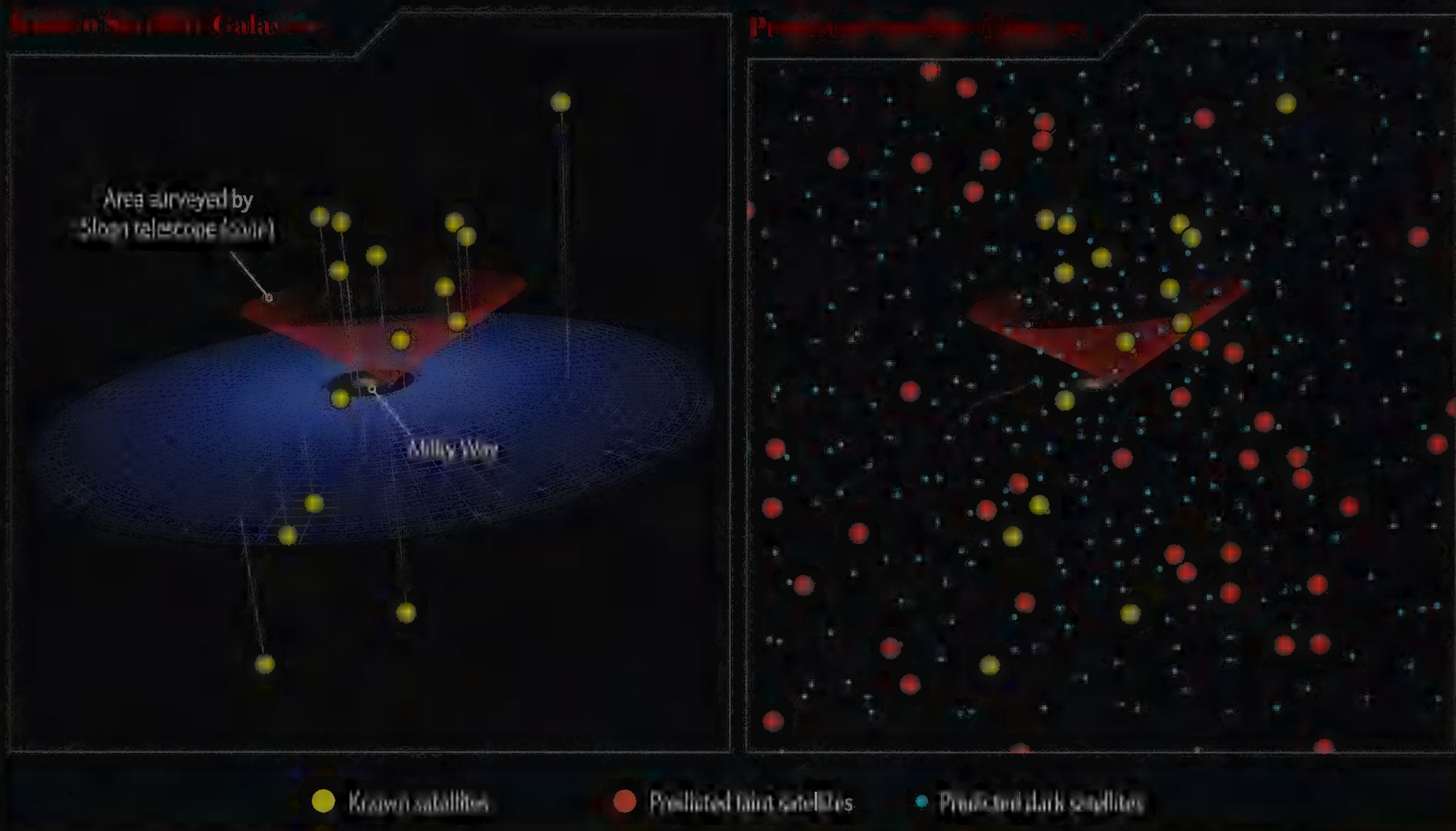
If the dark galaxy is massive enough, a method devised by Sukanya Chakrabarti, now at Florida Atlantic University, and several collaborators, including myself, may provide the tools to discern its passage. We recently showed that the largest disturbances in the outskirts of galaxies are often tidal imprints left by passing galaxies, which can be differentiated from other perturbations. By analyzing the disturbances, we can infer both the mass and current location of the intrusive galaxy. This technique can discern galaxies as small as one-thousandth the mass of the primary galaxy. Applying this method to the Milky Way, our team inferred that an undiscovered possibly dark galaxy lurks in the plane of the Milky Way, about 300,000 light-years from the galactic center. Plans are now under way to hunt for this galaxy in near-infrared light using data collected by the Spitzer Space Telescope.

TOO LITTLE LIGHT

QUITE APART from the challenge of finding them, ultrafaint and dark galaxies in the Milky Way's vicinity pose a deeper problem for astronomers in regard to the relative amounts of material they contain. Astronomers commonly measure the amount of matter in a galaxy in terms of its mass-to-light ratio: the mass of material divided by the total amount of light it gives off. Typically we give the ratio in solar units; the sun, by definition, has

Lost Sheep of the Galactic Family

Theories predict our Milky Way should be orbited by hundreds of satellite galaxies. Astronomers have long worried they could find only two dozen or so, but new searches using the Sloan Digital Sky Survey have closed the gap by spotting previously unseen satellites. They are composed almost entirely of dark matter. (The positions of the predicted satellites are schematic, reflecting their overall distribution.)



SOURCE: JAMES BULLOCK University of California, Irvine (known satellites)

a mass-to-light ratio of 1. In our galaxy, the average star is somewhat less massive and much dimmer than the sun, so the overall mass-to-light ratio of luminous matter is closer to 3. Including dark matter, the total mass-to-light ratio of the Milky Way jumps to about 30.

Josh Simon, now at the Carnegie Institution of Washington, and Marla Geha, now at Yale University, measured the velocities of the stars in eight ultrafaint dwarfs to obtain the mass and luminosity of these galaxies. The mass-to-light ratios in some cases exceed 1,000—by far the highest of any structure in the known universe. In the universe as a whole, the ratio of dark to ordinary matter is almost exactly 5. Why is the mass-to-light ratio of the Milky Way system so much higher and the ultrafaint galaxies even more so?

The answer could lie in the numerator or denominator of the ratio: galaxies with mass-to-light ratios higher than the universal average either have more mass than expected or produce less light. Astronomers think that the denominator is to blame. A huge amount of ordinary matter does not radiate brightly enough to see, either because it has never been able to settle into galaxies and coalesce into stars or because it did settle into galaxies but was then expelled back out into intergalactic space, where it resides in an ionized form that is undetectable by present-day telescopes [see "The Lost Galaxies," by James E. Geach; Scientific American, May]. Lower-mass galaxies, having weaker gravity, lose more of their gas, so their light output is disproportionately reduced. What a curious irony that the problems raised by one kind of unseen matter (dark matter) should give rise to yet another set (ordinary but undetected matter).

The puzzle of dark matter, which lay dormant for so many years, is now one of the most vibrant research areas in both physics and astronomy. Physicists are hoping to identify and detect the particle that composes dark matter, and astronomers are looking for more clues about how the stuff behaves. But puzzle or no, the existence of dark matter has provided the answer to a large range of astronomical phenomena. ■

MORE TO EXPLORE

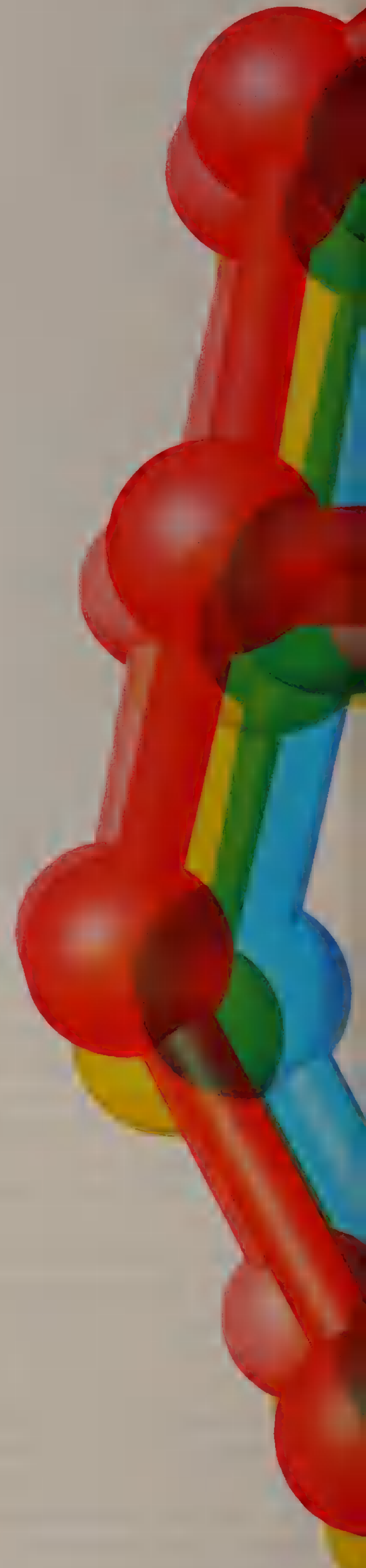
A Magellanic Origin for the Warp of the Galaxy. Martin D. Weinberg and Leo Blitz in *Astrophysical Journal Letters*, Vol. 641, No. 1, pages L33–L36; April 10, 2006. http://arxiv.org/abs/astro-ph/0601694

The Vertical Structure of the Outer Milky Way H I Disk. E. S. Levine, Leo Blitz and Carl Heiles in *Astrophysical Journal*, Vol. 643, No. 2, pages 881–896; June 1, 2006. http://arxiv.org/abs/astro-ph/0601697

Finding Dark Galaxies from Their Tidal Imprints. Sukanya Chakrabarti, Frank Bigiel, Philip Chang and Leo Blitz. Submitted to *Astrophysical Journal*. http://arxiv.org/abs/1101.0815

SCIENTIFIC AMERICAN ONLINE
For animated versions of the diagrams in this article, including a 3-D tour of the Milky Way, visit ScientificAmerican.com/oct2011/blitz

A-T-O-M P-O-W-E-R

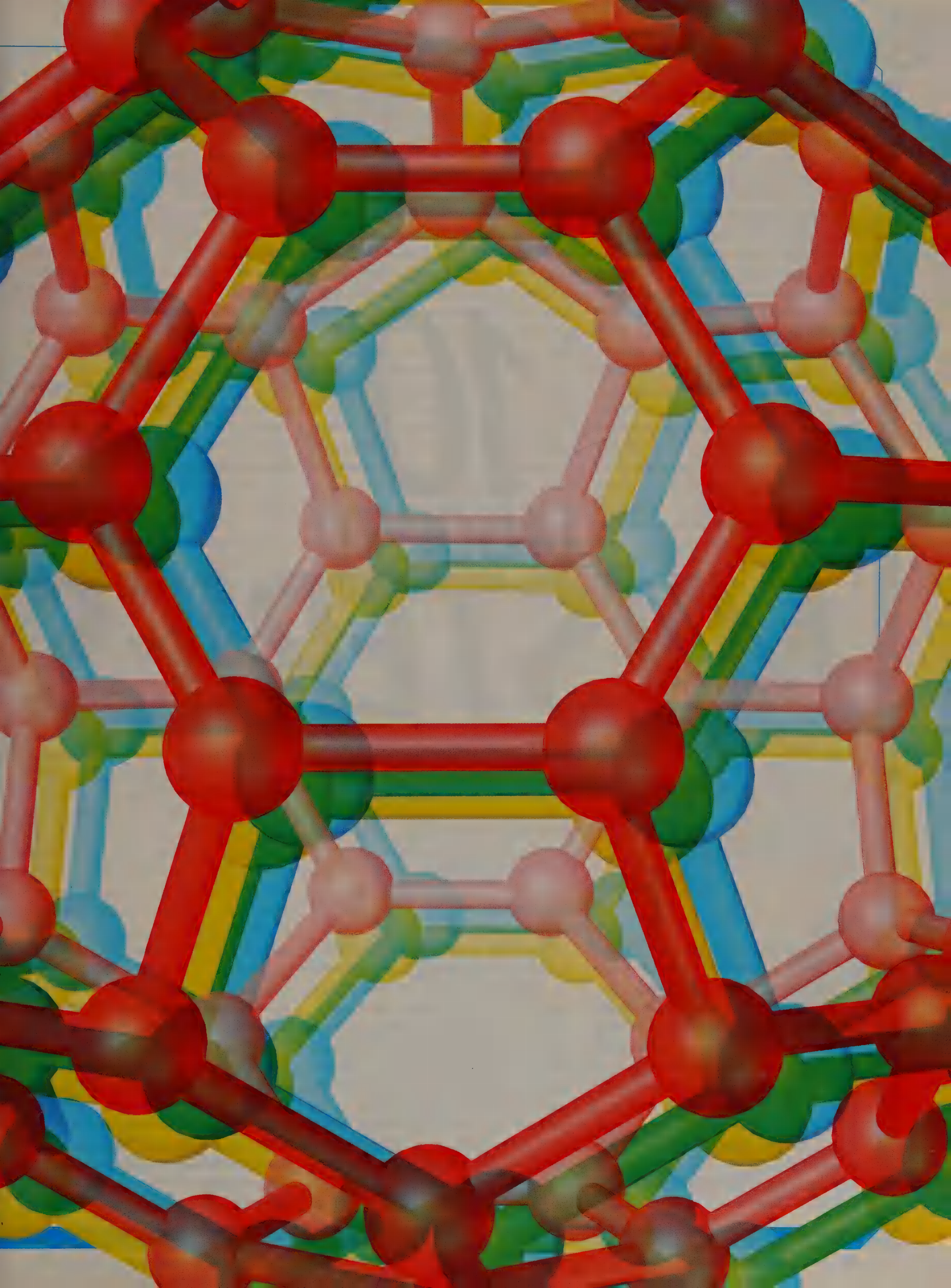


2011 is the International Year of Chemistry— a well-deserved celebration of that science's profound power

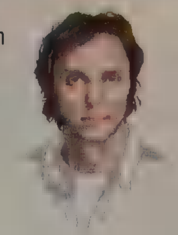
The popular idea that chemistry is now conceptually understood and that all we have to do is use it is false. Sure, most of the products we use in our daily lives were made possible by modern chemistry. But producing useful compounds is far from all chemists do. In fact, many of the most pressing problems of modernity—from making cars cleaner to altering the fate of living cells—are, at heart, problems in chemistry and will require chemists to solve them. So, too, will some of the most fundamental mysteries in science.

The International Year, a United Nations designation, has the theme of "chemistry—our life, our future" and is being honored with a range of activities globally. Our own celebration follows. Learn about 10 open questions that all have chemistry at their core and about the surprising role of chemical signaling in human interactions. These stories underscore how far and deep the science of chemistry reaches into our modern life. *—The Editors*

Illustration by George Retseck



Philip Ball has a Ph.D. in physics from the University of Bristol in England and was an editor at *Nature* for more than 20 years. He is the award-winning author of 15 books, including *The Music Instinct: How Music Works, and Why We Can't Do without It.*



CHEMISTRY

10 UNSOLVED MYSTERIES

Many of the most profound scientific questions—and some of humanity's most urgent problems—pertain to the science of atoms and molecules

By Philip Ball

1 How Did Life Begin?

THE MOMENT WHEN the first living beings arose from inanimate matter almost four billion years ago is still shrouded in mystery. How did relatively simple molecules in the primordial broth give rise to more and more complex compounds? And how did some of those compounds begin to process energy and replicate (two of the defining characteristics of life)? At the molecular level, all of those steps are, of course, chemical reactions, which makes the question of how life began one of chemistry.

The challenge for chemists is no longer to come up with vaguely plausible scenarios, of which there are plenty. For example, researchers have speculated about minerals such as clay acting as catalysts for the formation of the first self-replicating polymers (molecules that, like DNA or proteins, are long chains of smaller units); about chemical complexity fueled by the energy of deep-sea hydrothermal vents; and about an "RNA world," in which DNA's cousin RNA—which can act as an enzyme and catalyze reactions the way proteins do—would have been a universal molecule, before DNA and proteins appeared.

No, the game is to figure out how to test these ideas in reactions coddled in the test tube. Researchers have shown, for example, that certain relatively simple chemicals can spontaneously react to form the more complex building blocks of living systems, such as amino acids and nucleotides, the basic units of DNA and RNA. In 2009 a team led by John Sutherland, now at the MRC Laboratory of Molecular Biology in Cambridge, England, was able to demonstrate the formation of nucleotides from molecules likely

to have existed in the primordial broth. Other researchers have focused on the ability of some RNA strands to act as enzymes, providing evidence in support of the RNA world hypothesis. Through such steps, scientists may progressively bridge the gap from inanimate matter to self-replicating, self-sustaining systems.

Now that scientists have a better view of strange and potentially fertile environments in our solar system—the occasional flows of water on Mars, the petrochemical seas of Saturn's moon Titan, and the cold, salty oceans that seem to lurk under the ice of Jupiter's moons Europa and Ganymede—the origin of terrestrial life seems only a part of grander questions: Under what circumstances can life arise? And how widely can its chemical basis vary? That issue is made richer still by the discovery, over the past 16 years, of more than 500 extrasolar planets orbiting other stars—worlds of bewildering variety.

These discoveries have pushed chemists to broaden their imagination about the possible chemistries of life. For instance, NASA has long pursued the view that liquid water is a prerequisite, but now scientists are not so sure. How about liquid ammonia, formamide, an oily solvent like liquid methane or supercritical hydrogen on Jupiter? And why should life restrict itself to DNA, RNA and proteins? After all, several artificial chemical systems have now been made that exhibit a kind of replication from the component parts without relying on nucleic acids. All you need, it seems, is a molecular system that can serve as a template for making a copy and then detach itself.

Looking at life on Earth, says chemist Steven Benner of the Foundation for Applied Molecular Evolution in Gainesville, Fla., "we have no way to decide whether the similarities [such as the use of DNA and proteins] reflect common ancestry or the needs of life universally." But if we retreat into saying that we have to stick with what we know, he says, "we have no fun."

2 How Do Molecules Form?

MOLECULAR STRUCTURES may be a mainstay of high school science classes, but the familiar picture of balls and sticks representing atoms and the bonds among them is largely a conventional fiction. The trouble is that scientists disagree on what a more accurate representation of molecules should look like.

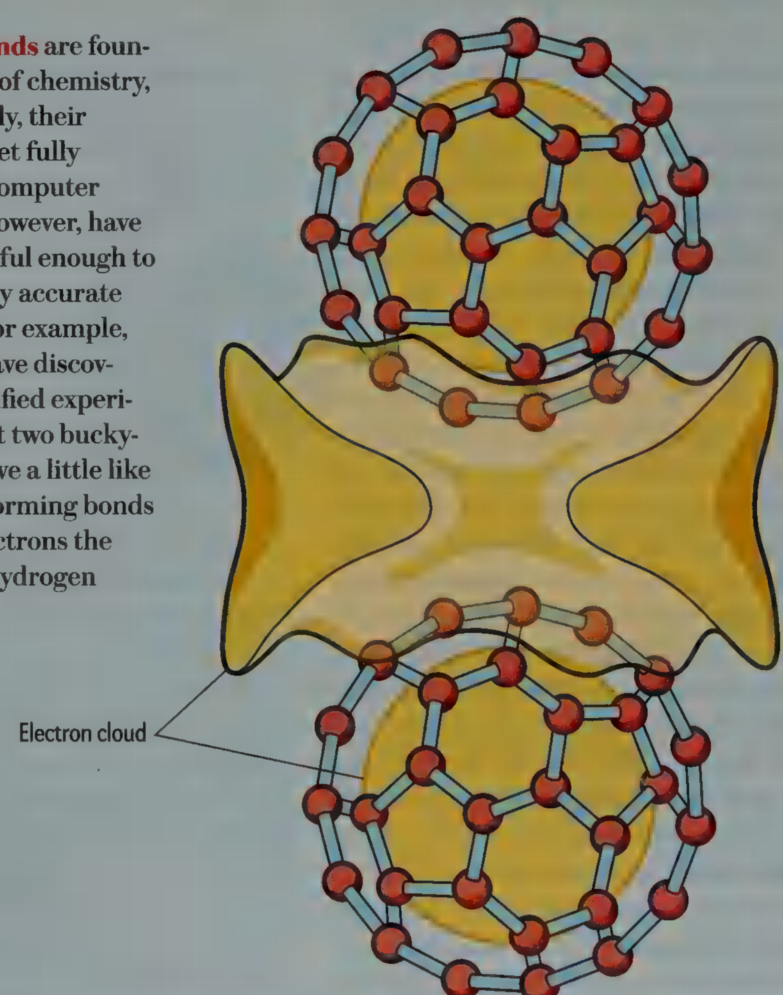
In the 1920s physicists Walter Heitler and Fritz London showed how to describe a chemical bond using the equations of then nascent quantum theory, and the great American chemist Linus Pauling proposed that bonds form when the electron orbitals of different atoms overlap in space. A competing theory by Robert Mulliken and Friedrich Hund suggested that bonds are the result of atomic orbitals merging into "molecular orbitals" that extend over more than one atom. Theoretical chemistry seemed about to become a branch of physics.

Nearly 100 years later the molecular-orbital picture has become the most common one, but there is still no consensus among chemists that it is always the best way to look at molecules. The reason is that this model of molecules and all others are based on simplifying assumptions and are thus approximate, partial descriptions. In reality, a molecule is a bunch of atomic nuclei in a cloud of electrons, with opposing electrostatic forces fighting a constant tug-of-war with one another, and all components constantly moving and reshuffling. Existing models of the molecule usually try to crystallize such a dynamic entity into a static one and may capture some of its salient properties but neglect others.

Quantum theory is unable to supply a unique definition of chemical bonds that accords with the intuition of chemists whose daily business is to make and break them. There are now many ways of describing molecules as atoms joined by bonds. According to quantum chemist Dominik Marx of Ruhr University Bochum in Germany, pretty much all such descriptions "are useful in some cases but fail in others."

Computer simulations can now calculate the structures and properties of molecules from quantum first principles with great accuracy—as long as the number of electrons is relatively small. "Computational chemistry can be pushed to the level of utmost realism and complexity," Marx says. As a result, computer calculations can increasingly be regarded as a kind of virtual experiment that predicts the course of a reaction. Once the reaction to be simulated involves more than a few dozen electrons, however, the

Molecular bonds are foundational to all of chemistry, but surprisingly, their nature is not yet fully understood. Computer simulations, however, have become powerful enough to give reasonably accurate predictions. For example, researchers have discovered—and verified experimentally—that two buckyballs can behave a little like giant atoms, forming bonds by sharing electrons the way that two hydrogen atoms do.



calculations quickly begin to overwhelm even the most powerful supercomputer, so the challenge will be to see whether the simulations can scale up—whether, for example, complicated biomolecular processes in the cell or sophisticated materials can be modeled this way.

3 How Does the Environment Influence Our Genes?

THE OLD IDEA OF BIOLOGY was that who you are is a matter of which genes you have. It is now clear that an equally important issue is which genes you use. Like all of biology, this issue has chemistry at its core.

The cells of the early embryo can develop into any tissue type. But as the embryo grows, these so-called pluripotent stem cells differentiate, acquiring specific roles (such as blood, muscle or nerve cells) that remain fixed in their progeny. The formation of the human body is a matter of chemically modifying the stem cells' chromosomes in ways that alter the arrays of genes that are turned on and off.

One of the revolutionary discoveries in research on cloning and stem cells, however, is that this modification is reversible and can be influenced by the body's experiences. Cells do not permanently disable genes during differentiation, retaining only those they need in a "ready to work" state. Rather the genes that get switched off retain a latent ability to work—to give rise to the proteins they encode—and can be reactivated, for instance, by exposure to certain chemicals taken in from the environment.

What is particularly exciting and challenging for chemists is that the control of gene activity seems to involve chemical events happening at size scales greater than those of atoms and molecules—at the so-called mesoscale—with large molecular groups and assemblies interacting. Chromatin, the mixture of DNA and proteins that makes up chromosomes, has a hierarchical structure. The double helix is wound around cylindrical particles made from proteins called histones, and this string of beads is then bundled up into higher-order structures that are poorly understood [*see illustration on opposite page*]. Cells exercise great control over this packing—how and where a gene is packed into chromatin may determine whether it is active or not.

Cells have specialized enzymes for reshaping chromatin structure, and these enzymes have a central role in cell differentiation. Chromatin in embryonic stem cells seems to have a much looser, open structure: as some genes fall inactive, the chromatin becomes increasingly lumpy and organized. "The chromatin seems to fix and maintain or stabilize the cells' state," says pathologist Bradley Bernstein of Massachusetts General Hospital.

What is more, such chromatin sculpting is accompanied by chemical modification of both DNA and histones. Small molecules attached to them act as labels that tell the cellular machinery to silence genes or, conversely, free them for action. This labeling is called "epigenetic" because it does not alter the information carried by the genes themselves.

The question of the extent to which mature cells can be returned to pluripotency—whether they are as good as true stem cells, which is a vital issue for their use in regenerative medicine—seems to hinge largely on how far the epigenetic marking can be reset.

It is now clear that beyond the genetic code that spells out many of the cells' key instructions, cells speak in an entirely separate chemical language of genetics—that of epigenetics. "People can have a genetic predisposition to many diseases, including cancer, but whether or not the disease manifests itself will often depend on environmental factors operating through these epigenetic pathways," says geneticist Bryan Turner of the University of Birmingham in England.

4 How Does the Brain Think and Form Memories?

THE BRAIN is a chemical computer. Interactions between the neurons that form its circuitry are mediated by molecules: specifically, neurotransmitters that pass across the synapses, the contact points where one neural cell wires up to another. This chemistry of the mind is perhaps at its most impressive in the operation of memory, in which abstract principles and concepts—a telephone number, say, or an emotional association—are imprinted in states of the neural network by sustained chemical signals. How does chemistry create a memory that is both persistent and dynamic, as well as able to recall, revise and forget?

We now know parts of the answer. A cascade of biochemical processes, leading to a change in the amounts of neurotransmitter molecules in the synapse, triggers learning for habitual reflexes. But even this simple aspect of learning has short- and long-term stages. Meanwhile more complex so-called declarative memory (of people, places, and so on) has a different mechanism and location in the brain, involving the activation of a protein called the NMDA receptor on certain neurons. Blocking this receptor with drugs prevents the retention of many types of declarative memory.

Our everyday declarative memories are often encoded through a process called long-term potentiation, which involves NMDA receptors and is accompanied by an enlargement of the neuronal region that forms a synapse. As the synapse grows, so does the "strength" of its connection with neighbors—the voltage induced at the synaptic junction by arriving nerve impulses. The biochemistry of this process has been clarified in the past several years. It involves the formation of filaments within the neuron made from the protein actin—part of the basic scaffolding of the cell and the material that determines its size and shape. But that process can be undone during a short period before the change is consolidated if biochemical agents prevent the newly formed filaments from stabilizing.

Once encoded, long-term memory for both simple and complex learning is actively maintained by switching on genes that give rise to particular proteins. It now appears that this process can involve a type of molecule called a prion. Prions are proteins that can switch between two different conformations. One of the conformations is soluble, whereas the other is insoluble and acts as a catalyst to switch other molecules like it to the insoluble state, leading these molecules to aggregate. Prions were first discovered for their role in neurodegenerative conditions such as mad cow disease, but prion mechanisms have now been found to have beneficial functions, too: the formation of a prion aggregate marks a particular synapse to retain a memory.

There are still big gaps in the story of how memory works, many of which await filling with the chemical details. How, for example, is memory recalled once it has been stored? "This is a deep problem whose analysis is just beginning," says

neuroscientist and Nobel laureate Eric Kandel of Columbia University.

Coming to grips with the chemistry of memory offers the enticing and controversial prospect of pharmacological enhancement. Some memory-boosting substances are already known, including sex hormones and synthetic chemicals that act on receptors for nicotine, glutamate, serotonin and other neurotransmitters. In fact, according to neurobiologist Gary Lynch of the University of California, Irvine, the complex sequence of steps leading to long-term learning and memory means that there are many potential targets for such memory drugs.

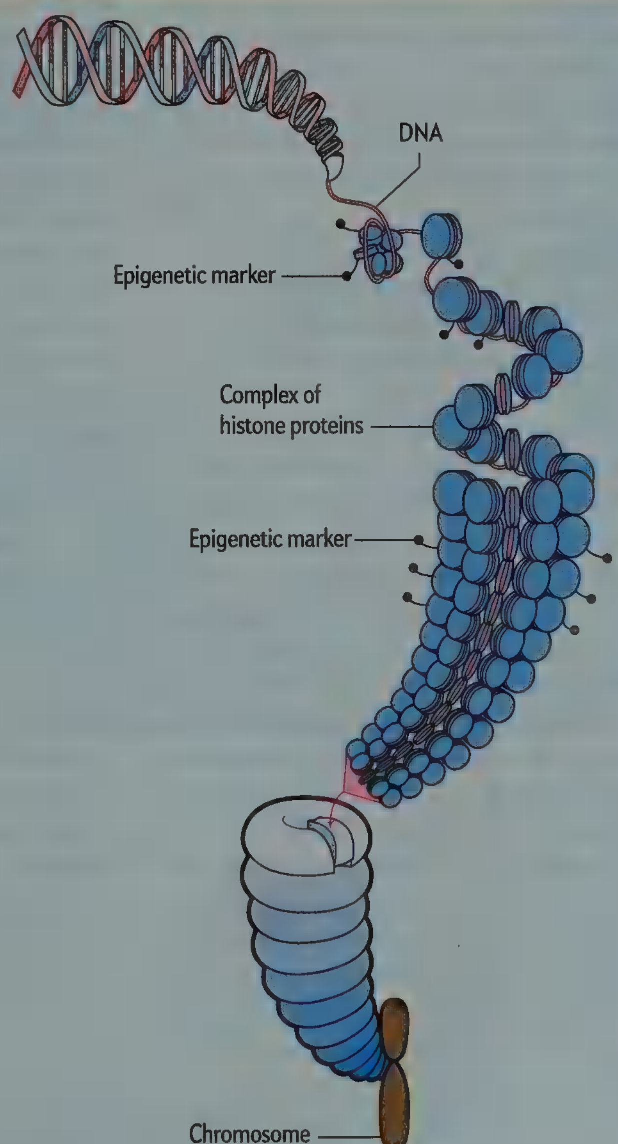
5 How Many Elements Exist?

THE PERIODIC TABLES that adorn the walls of classrooms have to be constantly revised, because the number of elements keeps growing. Using particle accelerators to crash atomic nuclei together, scientists can create new "superheavy" elements, which have more protons and neutrons in their nuclei than do the 92 or so elements found in nature. These engorged nuclei are not very stable—they decay radioactively, often within a tiny fraction of a second. But while they exist, the new synthetic elements such as seaborgium (element 106) and hassium (element 108) are like any other insofar as they have well-defined chemical properties. In dazzling experiments, researchers have investigated some of those properties in a handful of elusive seaborgium and hassium atoms during the brief instants before they fell apart.

Such studies probe not just the physical but also the conceptual limits of the periodic table: Do superheavy elements continue to display the trends and regularities in chemical behavior that make the table periodic in the first place? The answer is that some do, and some do not. In particular, such massive nuclei hold on to the atoms' innermost electrons so tightly that the electrons move at close to the speed of light. Then the effects of special relativity increase the electrons' mass and may play havoc with the quantum energy states on which their chemistry—and thus the table's periodicity—depends.

Because nuclei are thought to be stabilized by particular "magic numbers" of protons and neutrons, some researchers hope to find what they call the island of stability, a region a little beyond the current capabilities of element synthesis in which superheavies live longer. Yet is there any fundamental limit to their size? A simple calculation suggests that relativity prohibits electrons from being bound to nuclei of more than 137 protons. More sophisticated calculations defy that limit. "The periodic system will not end at 137; in fact, it will never end," insists nuclear physicist Walter Greiner of the Johann Wolfgang Goethe University Frankfurt in Germany. The experimental test of that claim remains a long way off.

Beyond genes, another set of instructions influences which genes are active in a cell. This epigenetic code conveys information through chemicals attached to DNA or to the histone proteins that DNA winds around in chromosomes. The chemical markers help to determine whether a gene is hidden away in a highly condensed part of the chromosomes or is accessible for transcription.



6 Can Computers Be Made Out of Carbon?

COMPUTER CHIPS made out of graphene—a web of carbon atoms—could potentially be faster and more powerful than silicon-based ones. The discovery of graphene garnered the 2010 Nobel Prize in Physics, but the success of this and other forms of carbon nanotechnology might ultimately depend on chemists' ability to create structures with atomic precision.

The discovery of buckyballs—hollow, cagelike molecules made entirely of carbon atoms—in 1985 was the start of something literally much bigger. Six years later tubes of carbon atoms arranged in a chicken wire–shaped, hexagonal pattern like that in the carbon sheets of graphite made their debut. Being hollow, extremely strong and stiff, and electrically conducting, these carbon nanotubes promised applications ranging from high-strength carbon composites to tiny wires and electronic devices, miniature molecular capsules, and water-filtration membranes.

For all their promise, carbon nanotubes have not resulted in a lot of commercial applications. For instance, researchers have not been able to solve the problem of how to connect tubes into

complicated electronic circuits. More recently, graphite has moved to center stage because of the discovery that it can be separated into individual chicken wire–like sheets, called graphene, that could supply the fabric for ultraminiaturized, cheap and robust electronic circuitry. The hope is that the computer industry can use narrow ribbons and networks of graphene, made to measure with atomic precision, to build chips with better performance than silicon-based ones.

"Graphene can be patterned so that the interconnect and placement problems of carbon nanotubes are overcome," says carbon specialist Walt de Heer of the Georgia Institute of Technology. Methods such as etching, however, are too crude for patterning graphene circuits down to the single atom, de Heer points out, and as a result, he fears that graphene technology currently owes more to hype than hard science. Using the techniques of organic chemistry to build up graphene circuits from the bottom up—linking together "polyaromatic" molecules containing several hexagonal carbon rings, like little fragments of a graphene sheet—might be the key to such precise atomic-scale engineering and thus to unlocking the future of graphene electronics.

7 How Do We Tap More Solar Energy?

WITH EVERY SUNRISE comes a reminder that we currently tap only a pitiful fraction of the vast clean-energy resource that is the sun. The main problem is cost: the expense of conventional photovoltaic panels made of silicon still restricts their use. Yet life on Earth, almost all of which is ultimately solar-powered by photosynthesis, shows that solar cells do not have to be terribly efficient if, like leaves, they can be made abundantly and cheaply enough.

"One of the holy grails of solar-energy research is using sunlight to produce fuels," says Devens Gust of Arizona State University. The easiest way to make fuel from solar energy is to split water to produce hydrogen and oxygen gas. Nathan S. Lewis and his collaborators at Caltech are developing an artificial leaf that would do just that [*see illustration on opposite page*] using silicon nanowires.

Earlier this year Daniel Nocera of the Massachusetts Institute of Technology and his co-workers unveiled a silicon-based membrane in which a cobalt-based photocatalyst does the water splitting. Nocera estimates that a gallon of water would provide enough fuel to power a home in developing countries for a day. "Our goal is to make each home its own power station," he says.

Splitting water with catalysts is still tough. "Cobalt catalysts such as the one that Nocera uses and newly discovered catalysts based on other common metals are promising," Gust says, but no one has yet found an ideal inexpensive catalyst. "We don't know how the natural photosynthetic catalyst, which is based on four manganese atoms and a calcium atom, works," Gust adds.

Gust and his colleagues have been looking into making molecular assemblies for artificial photosynthesis that more closely mimic their biological inspiration, and his team has managed to synthesize some of the elements that could go into such an assembly. Still, a lot more work is needed on this front. Organic molecules such as the ones nature uses tend to break down quickly. Whereas plants continually produce new proteins to replace broken ones, artificial leaves do not (yet) have the full chemical-synthesis machinery of a living cell at their disposal.

8 What Is the Best Way to Make Biofuels?

INSTEAD OF MAKING FUELS by capturing the rays of the sun, how about we let plants store the sun's energy for us and then turn plant matter into fuels? Biofuels such as ethanol made from corn and biodiesel made from seeds have already found a place in the energy markets, but they threaten to displace food crops, particularly in developing countries where selling biofuels abroad can be more lucrative than feeding people at home. The numbers are daunting: meeting current oil demand would mean requisitioning huge areas of arable land.

Turning food into energy, then, may not be the best approach. One answer could be to exploit other, less vital forms of biomass. The U.S. produces enough agricultural and forest residue to supply nearly a third of the annual consumption of gasoline and diesel for transportation.

Converting this low-grade biomass into fuel requires breaking down hardy molecules such as lignin and cellulose, the main building blocks of plants. Chemists already know how to do that, but the existing methods tend to be too expensive, inefficient or difficult to scale up for the enormous quantities of fuel that the economy needs.

One of the challenges of breaking down lignin—cracking open the carbon-oxygen bonds that link "aromatic," or benzene-type, rings of carbon atoms—was recently met by John Hartwig and Alexey Sergeev, both at the University of Illinois. They found a nickel-based catalyst able to do it. Hartwig points out that if biomass is to supply nonfossil-fuel chemical feedstocks as well as fuels, chemists will also need to extract aromatic compounds (those having a backbone of aromatic rings) from it. Lignin is the only major potential source of such aromatics in biomass.

To be practical, such conversion of biomass will, moreover, need to work with mostly solid biomass and convert it into liquid fuels for easy transportation along pipelines. Liquefaction would need to happen on-site, where the plant is harvested. One of the difficulties for catalytic conversion is the extreme impurity of the raw material—classical chemical synthesis does not usually deal with messy materials such as wood. "There's no consensus on how all this will be done in the end," Hartwig says. What is certain is that an awful lot of any solution lies with the chemistry, especially with finding the right catalysts. "Almost every industrial reaction on a large scale has a catalyst associated" with it, Hartwig points out.

9 Can We Devise New Ways to Create Drugs?

THE CORE BUSINESS of chemistry is a practical, creative one: making molecules, a key to creating everything from new materials to new antibiotics that can outstrip the rise of resistant bacteria.

In the 1990s one big hope was combinatorial chemistry, in which thousands of new molecules are made by a random assembly of building blocks and then screened to identify those that do a job well. Once hailed as the future of medicinal chemistry, "combi-chem" fell from favor because it produced little of any use.

But combinatorial chemistry could enjoy a brighter second phase. It seems likely to work only if you can make a wide enough range of molecules and find good ways of picking out the minuscule

amounts of successful ones. Biotechnology might help here—for example, each molecule could be linked to a DNA-based "bar code" that both identifies it and aids its extraction. Or researchers can progressively refine the library of candidate molecules by using a kind of Darwinian evolution in the test tube. They can encode potential protein-based drug molecules in DNA and then use error-prone replication to generate new variants of the successful ones, thereby finding improvements with each round of replication and selection.

Other new techniques draw on nature's mastery at uniting molecular fragments in prescribed arrangements. Proteins, for example, have a precise sequence of amino acids because that sequence is spelled out by the genes that encode the proteins. Using this model, future chemists might program molecules to assemble autonomously. The approach has the advantage of being "green" in that it reduces the unwanted by-products typical of traditional chemical manufacturing and the associated waste of energy and materials.

David Liu of Harvard University and his co-workers are pursuing this approach. They tagged the building blocks with short DNA strands that program the linker's structure. They also created a molecule that walks along that DNA, reading its codes and sequentially attaching small molecules to the building block to make the linker—a process analogous to protein synthesis in cells. Liu's method could be a handy way to tailor new drugs. "Many molecular life scientists believe that macromolecules will play an increasingly central, if not dominant, role in the future of therapeutics," Liu says.

10 Can We Continuously Monitor Our Own Chemistry?

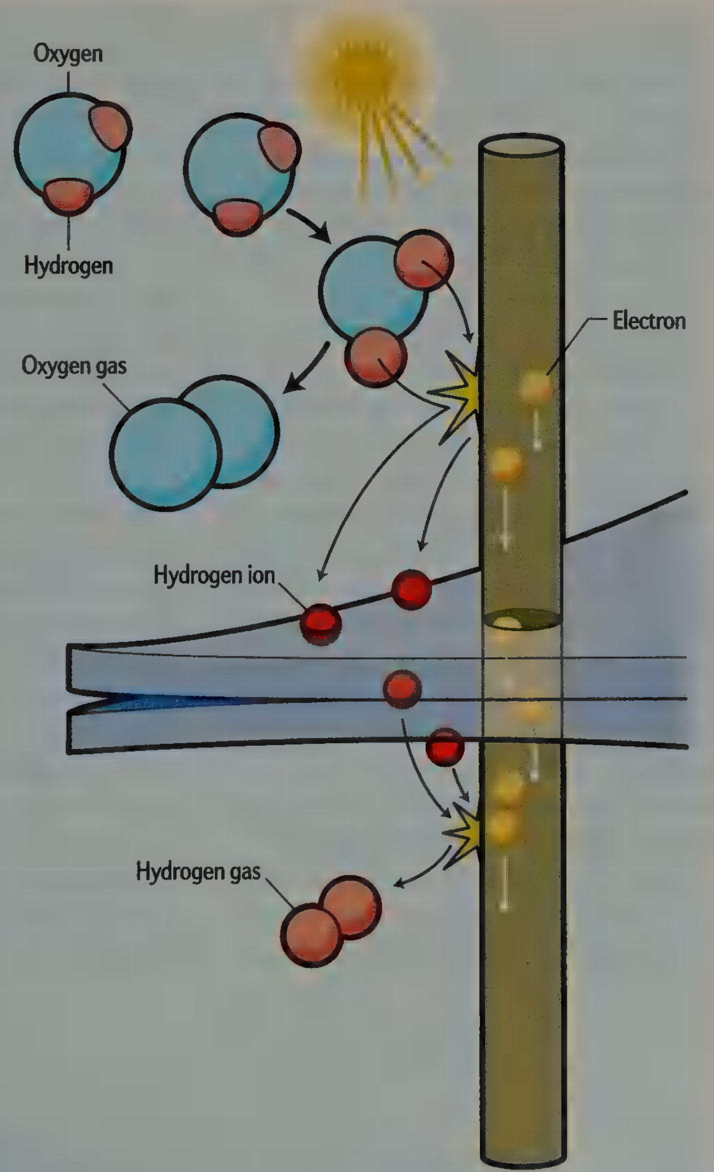
INCREASINGLY, chemists do not want to just make molecules but also to communicate with them: to make chemistry an information technology that will interface with anything from living cells to conventional computers and fiber-optic telecommunications.

In part, it is an old idea: biosensors in which chemical reactions are used to report on concentrations of glucose in the blood date back to the 1960s, although only recently has their use for monitoring diabetes been cheap, portable and widespread. Chemical sensing could have countless applications—to detect contaminants in food and water at very low concentrations, for instance, or to monitor pollutants and trace gases present in the atmosphere. Faster, cheaper, more sensitive and more ubiquitous chemical sensing would yield progress in all of those areas.

It is in biomedicine, though, that new kinds of chemical sensors would have the most dramatic potential. For instance, some of the products of cancer genes circulate in the bloodstream long before the condition becomes apparent to regular clinical tests. Detecting these chemicals early might make prognoses more timely and accurate. Rapid genomic profiling would enable drug regimens to be tailored to individual patients, thereby reducing risks of side effects and allowing some medicines to be used that today are hampered by their dangers to a genetic minority.

Some chemists foresee continuous, unobtrusive monitoring of all manner of biochemical markers of health and disease, perhaps providing real-time information to surgeons during operations or to automated systems for delivering remedial drug treatments. This futuristic vision depends on developing chemical methods for selectively sensing particular substances and signaling about them even when the targets occur in only very low concentrations. ■

Mimicking plants, chemists are developing new catalysts and materials to capture solar energy and store it as hydrogen gas. Here nanowires exposed to sunlight split water molecules into hydrogen ions, oxygen atoms and electrons. The ions and the electrons travel down to the other side of a membrane. Then the nanowires catalyze the formation of hydrogen gas from the electrons and ions.



MORE TO EXPLORE

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BIOCHEMISTRY

THE SCENT OF YOUR THOUGHTS

Although we are usually unaware of it, we communicate through chemical signals just as much as birds and bees do

By Deborah Blum

Deborah Blum won a Pulitzer Prize in 1992 and is author most recently of *The Poisoner's Handbook: Murder and the Birth of Forensic Medicine in Jazz Age New York.* She first learned about pheromones by watching her father, an entomologist, extract them from ants.

THE MOMENT THAT STARTED MARTHA MCCLINTOCK'S SCIENTIFIC CAREER WAS A WHIM OF youth. Even, she recalls, a ridiculous moment. It is summer, 1968, and she is a Wellesley College student attending a workshop at the Jackson Laboratory in Maine. A lunch-table gathering of established researchers is talking about how mice appear to synchronize their ovary cycles. And 20-year-old McClintock, sitting nearby, pipes up with something like, "Well, don't you know? Women do that, too."

"I don't remember the exact words," she says now, sitting relaxed and half-amused in her well-equipped laboratory at the University of Chicago. "But everyone turned and stared." It is easy to imagine her in that distant encounter—the same direct gaze, the same friendly face and fly-away hair. Still, the lunch-table group is not charmed; it informs her that she does not know what she is talking about.

Undaunted, McClintock raises the question with some graduate students who are also attending the workshop. They bet that she will not be able to find data to support her assertion. She returns to Wellesley and talks this matter over with her undergraduate adviser, Patricia Sampson. And Sampson throws it back at her: take the bet, do the research, prove yourself right or wrong.

Three years later, now a graduate student, McClintock publishes a two-page paper entitled "Menstrual Synchrony and Suppression" in the journal *Nature.* (*Scientific American* is part of Nature Publishing Group.) It details a rather fascinating effect seen in some 135 residents of Wellesley dormitories during an academic year. In that span, menstrual cycles apparently began to shift, especially among women who spent a lot of time together. Menstruation became more synchronized, with more overlap of when it started and finished.

Today the concept of human menstrual synchronization is generally known as the McClintock effect. But the idea that has continued to shape both her research and her reputation, the one that drives a still flourishing field of research, is that this mysterious synchrony, this reproductive networking, is caused by chemical messaging between women—the notion that humans, like so many other creatures, reach out to one another with chemical signals.

It has been harder than expected to single out specific signaling chemicals and trace their effects on our bodies and minds as precisely as entomologists have done for countless insect pheromones. But in the four decades since McClintock's discovery, scientists have charted the influence of chemical signaling across a spectrum of human behaviors. Not only do we synchronize our reproductive cycles, we can also recognize our kin, respond to others' stress and react to their moods—such as fear or sadness or "not tonight, honey"—all by detecting chemicals they quietly secrete. As researchers learn more about this web of human interaction, they are helping to bridge an arbitrary dividing line between humans and the natural world.

ANIMAL KINGDOM CHEMISTRY

THE VERY INTRIGUING IDEA of animals sharing invisible chemical cues has a long and illustrious history, at least as far as other species are concerned. The ancient Greeks talked enthusiastically of the possibility that female dogs in heat might produce some mysterious secretion capable of driving male dogs into a panting frenzy. Charles Darwin, pointing to several famously smelly species, proposed that chemical signals were part of the sexual selection process. Throughout the late 19th

IN BRIEF

Evidence suggests that humans unconsciously exchange chemical messages that help to synchronize women's menstrual cycles, signify the presence of kin, and convey moods such as stress or fear.

The signals may be akin to the pheromones found in hundreds of animal species, including mammals.

Researchers are isolating the compounds secreted by humans and attempting to decode their physiological and psychological effects.

Illustration by Noma Bar

century the great French naturalist Jean-Henri Fabre puzzled over evidence that the siren call of chemistry could stir winged insects into determined flight.

Still, it was not until 1959 that the science really began to gain traction. In that year Adolf Butenandt, a Nobel laureate in chemistry, isolated and analyzed a compound that female silk moths release to attract males. Butenandt dissected the insects and painstakingly extracted the chemical from their microscopic secretion glands. He collected enough to crystallize it so that he could discern its molecular structure by x-ray crystallography. He called the compound "bombykol," after the Latin name for the silk moth.

It was the first known pheromone, although the term did not yet exist. Shortly after, two of Butenandt's colleagues, German biochemist Peter Karlson and Swiss entomologist Martin Lüscher, coined that name out of two Greek words: *pherein* (to transport) and *horman* (to stimulate). They defined a pheromone as a type of small molecule that carries chemical messages between individuals of the same species. The compounds must be active in very tiny amounts, potent below a conscious scent threshold. When released by one individual in a species and received by another, the two researchers wrote, they produce a measurable effect, "a specific reaction, for instance, a definite behavior or a developmental process."

Since then, an astonishing array of pheromones—the best known and established class of chemical-signaling molecules exchanged by animals—have been found in insects, not just in silk moths but in bark beetles, cabbage looper moths, termites, leaf-cutter ants, aphids and honeybees. According to a 2003 report from the National Academy of Sciences, entomologists "have now broken the code for the pheromone communication of more than 1,600 insects." And pheromones serve many more purposes than simply attracting mates: they elicit alarm, identify kin, alter mood, tweak relationships.

By the late 1980s pheromones had also been found to influence a wide spectrum of noninsect species, including lobsters, fish, algae, yeast, ciliates, bacteria, and more. As this new science of chemical communication grew—acquiring the more formal name of semiochemistry, from the Greek *semion* (meaning "signal")—scientists extended the search to mammals. Almost immediately they ran into resistance from their colleagues.

"In the 1970s and 1980s people would jump at you if you said 'mammalian pheromone,'" recalls Milos Novotny, director of the Institute for Pheromone Research at Indiana University. "They'd say, 'There's no such thing: mammals are not like insects. They're too evolved and complex to be spontaneously responding to something like a pheromone.'"

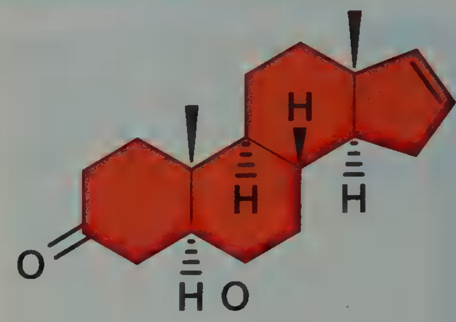
But by the mid-1980s Novotny had not only identified a pheromone in mice that regulated intermale aggression, he had synthesized it. Such compounds were also verified in rats, hamsters, rabbits and squirrels. And as the list lengthened, it also became apparent that mammals' pheromones were very like—if not identical—to those found in insects. As an example, most researchers cite the stunning work of the late Oregon Health and Science University biochemist L.E.L. "Bets" Rasmussen, who showed in 1996 that a sex pheromone secreted by female Asian elephants is chemically identical to one used by more than 100 species of moths for similar purposes of attraction.

McClintock had proposed a similar idea in 1971 in her pioneering paper on menstrual synchrony. "Perhaps," she wrote then, "at least one female pheromone affects the timing of other female menstrual cycles."

ODOROUS LANDSCAPE

MCCLINTOCK, NOW 63, is sitting in a small, sunny room occupied by filing cabinets, computers, racks of stoppered vials and tubes, and scent sticks—all contributing to a faint, slightly sweet chemical aroma—and a dark-haired graduate student named David Kern. ("All the other graduate students would climb over my dead body to get in this room," he says.) McClintock's lab is at the University of Chicago's Institute for Mind and Biology, of which she is a founding director. She wears a tweedy jacket over a bright, patterned shirt, and she is thinking over a question: How far has the science of semiochemistry traveled since that day, some four decades ago? The case for human chemical communication has been made, she says, and "our goal is to tackle identifying the chemical compounds. And then we can refine our understanding of what fundamental roles they play."

That task is anything but easy. Human body odor is estimated to derive from about 120 compounds. Most of these compounds occur in the water-rich solution produced by the sweat glands or are released from apocrine, or scent, glands in the oily shafts of hair follicles. The apocrine glands concentrate the most under the arms, around the nipples and in the genital regions.



The steroid androstadienone is a promising candidate for a human pheromone. It has been shown to influence cognition, stress hormones and emotional responses.

It is a complicated landscape, made even more complicated by our use of what researchers refer to as exogenous compounds, such as soap, deodorants and perfumes, as Johan Lundström of the Monell Chemical Senses Center in Philadelphia points out. And yet Lundström marvels at how adeptly our brains sort through this chemical tangle. Neuroimaging work done at his lab finds a 20 percent faster response to known human chemical signals compared with chemically similar molecules found elsewhere in the environment. "The brain always knows when it smells a body odor," Lundström says.

This capacity is already present in infancy. Numerous studies in humans have shown that, as is true in animals, mothers and infants are acutely attuned to each other's scent. This scent knowledge is so precise that babies even prefer the parts of clothes worn by their mother (and their mother only) touched by sweat compounds. The recognition, interestingly, is more acute in breast-fed infants than in those raised on baby formula.

"We're still just mapping the influential compounds from those that are not," Lundström says. "I don't think we're dealing with one single compound but rather a range of different ones that may be important at different times." Pheromones operate under the radar, he says, and they influence—but do not necessarily completely control—numerous behaviors. "If

Illustration by Brown Bird Design

we compare these with social cues, they may be less important than the obvious ways we communicate," Lundström says. But, he adds, the ability probably aided survival as we evolved, keeping us more closely attuned to one another.

Psychologist Denise Chen of Rice University also argues that this kind of chemical alertness would have conferred an evolutionary advantage. In her research, she collects odor samples from individuals while they watch horror movies. Gauze pads are kept in viewers' armpits to collect sweat released during moments of fear. Later, the pads are placed under volunteers' nostrils. For comparison, Chen has also collected sweat from people watching comedies or neutral films such as documentaries.

One of her early experiments found that participants could tell whether the sweat donor was fearful or happy at the time the sweat was produced. The subjects' guesses succeeded more often than they would by pure chance, especially for fear-induced sweat. Chen followed up with research showing that exposure to "fear sweat" seemed to intensify the alarm response—inclining participants to see fear in the faces of others. These exposures even enhanced cognitive performance: on word-association tests that included terms suggestive of danger, women smelling fear sweat outperformed those exposed to neutral sweat. "If you smell fear, you're faster at detecting fearful words," Chen explains.

In a study currently in press, she and Wen Zhou of the Chinese Academy of Sciences compared the response of long-time couples with people in shorter-term relationships. Those results indicated—perhaps not surprisingly—that the longer couples are together, the better the partners are at interpreting the fear or happiness information apparently encoded in sweat. "What I hope that people will see in this is that understanding olfaction is important for us to understand ourselves," Chen says.

And evidence continues to accumulate that unconscious perception of scents influences a range of human behaviors, from cognitive to sexual. In January, for instance, a team of scientists at Israel's Weizmann Institute of Science in Rehovot, led by psychologist Noam Sobel, reported that men who sniffed drops of women's emotional tears felt suddenly less sexually interested in comparison to those who smelled a saline solution. Sobel found a direct physical response to this apparent chemosignal: a small but measurable drop in the men's testosterone levels. The signal may have evolved to signify lower fertility, such as during menstruation. More generally, the discovery may help explain the uniquely human behavior of crying.

HARD SCIENCE

A MAJOR GOAL now is to identify the key chemicals that convey signals surreptitiously and to learn much more about how the body detects and reacts to those signals. George Preti, a Monell chemist, has mapped out a research project that would include tracking these messengers by analyzing sweat and apocrine secretions and studies of hormone levels in those who sniff the chemicals. "We've yet to identify the precise signals that carry the information," Lundström agrees. "And if we want a solid standing for this work, that's what's needed next."

McClintock also sees this as a priority. In recent years she has focused on building a detailed portrait of one of the more potent known chemosignals, a steroid compound called androstadienone. She believes that this particular small molecule is potent enough to meet the requirements of being called a human pheromone: it is a small molecule that acts as a same-species chemical signal and influences physiology and behavior. Over the years labs, including McClintock's and Lundström's, have found that this particular compound shows measurable effects on cognition and that it can alter levels of stress hormones such as cortisol and evoke changes in emotional response.

In one recent study McClintock and her colleague Suma Jacob of the University of Illinois at Chicago explored androstadienone's propensity to affect mood. They mixed a trace amount into the solvent propylene glycol and then masked any possible overt odor with oil of clove. They then exposed one study group to a solvent containing the compound and another to a plain solvent. Subjects were asked to smell gauze pads containing one version; they were told only that they were participating in olfaction research. All the subjects went on to fill out a long and tedious questionnaire.

Overall, the subjects exposed to androstadienone remained far more cheerful throughout the 15- to 20-minute test. A follow-up study repeated the same process but included brain imaging as well. The neuroimages showed that brain regions associated with attention, emotion and visual processing were more active in those exposed to the chemosignaling compound. McClintock sees this as a classic pheromonal effect, the kind that she speculated about decades ago.

Even so, she and other researchers continue to carefully talk of "putative" pheromones. Humans are complicated, and any causal links between specific chemicals and changes in behavior are hard to demonstrate conclusively. Indeed, no one can say for certain yet what chemical or chemicals account for McClintock's original discovery, the synchronization of women's menstrual cycles. Even the phenomenon itself has proved somewhat elusive: it has been confirmed in numerous follow-up studies but contradicted by others, and it is still not accepted unanimously by the scientific community.

Much of the discussion centers on what exactly is being synchronized—perhaps timing of ovulation, perhaps length of cycle. A review of human data from the 1990s by the father-and-son team of Leonard and Aron Weller of Bar-Ilan University in Israel found that synchrony sometimes occurs and sometimes does not. "If it exists," Leonard Weller reported, "it is certainly not ubiquitous."

Although she still retains the assertiveness of her college days, McClintock agrees that the effect is subtler than she thought at first. But she also believes that the critics tend to miss the more important point: that evidence for chemical communication between humans has steadily accumulated since her study. And that it is not surprising that our chemical messaging is turning out to be as intricate as every other form of human communication. ■

MORE TO EXPLORE

Menstrual Synchrony and Suppression. Martha McClintock in *Nature*, Vol. 229, pages 244–245; January 22, 1971.

Pheromones and Animal Behavior: Communication by Smell and Taste. Tristram D. Wyatt. Cambridge University Press, 2003.

Insect Pheromones: Mastering Communication to Control Pests. Margie Patlak et al. National Academy of Sciences, 2009.

Fifty Years of Pheromones. Tristram D. Wyatt in *Nature*, Vol. 457, pages 262–263; January 15, 2009.

SCIENTIFIC AMERICAN ONLINE
More International Year of Chemistry coverage at ScientificAmerican.com/oct2011/chemistry

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GEOLOGY

AFGHANISTAN'S BURIED RICHES

Geologists say newfound deposits in the embattled country could fulfill the world's desire for rare-earth and critical minerals and end opium's local stranglehold in the process

By Sarah Simpson

THE SCENE AT FIRST RESEMBLES MANY THAT play out daily in the war-torn Red Zone of southern Afghanistan: a pair of Black Hawk helicopters descend on a hillside near the country's southern border with Pakistan. As the choppers land, U.S. marines leap out, assault rifles ready. But then geologists sporting helmets and heavy ceramic vests jump out, too. The researchers are virtually indistinguishable from the soldiers except that they carry rock hammers instead of guns. A human chain of soldiers encircles the scientists as they step forward on the dusty ground.

"The minute you get off, you go into geologist mode," says Jack H. Medlin, director of the U.S. Geological Survey's activities in Afghanistan. "You forget, basically, that these guys are around—unless you try to get out of the circle."

Medlin's team has flown many missions, each one limited to an hour so that hostile forces do not have time to organize and descend. Sixty minutes is a stressful, fleeting instant to geologists who would typically take days to carefully sample and map a site. The rocks con-

IN BRIEF

Under military cover, U.S. geologists have mapped Afghanistan's deposits of critical minerals. Rich reserves of rare-earth elements exist in the south, where Taliban control is tightest.

If mining of important minerals can take off in the north, that success could create enormous commercial and political momentum for opening the south. New estimates indicate that rare earths could be triple the initial predictions.

Overcoming the country's opium and Taliban strongholds with a mining bonanza could change U.S. foreign policy and world stability.

Over the long term, Afghanistan's geologists will have to take charge. The U.S. Geological Survey is nearly done training them.

MOISES SAMAN *Redux Pictures*

[illegible] hills in southern Afghanistan could harbor enough rare-earth elements to supply the world for years.

taining a desirable element—say, gold or neodymium—are invariably sandwiched between less interesting ones, all of which were laid down long ago and since folded, buried and exhumed so that they protrude only here and there, possibly in deeply eroded streambeds or on opposite sides of a steep valley. Following the trail takes expertise, stamina and concentration. The marines know that their protégés pursue the clues like bloodhounds, so the human circle moves with the scientists.

The latest of these gutsy excursions, carried out in February, proved that the missions have been worth the risks. It revealed a superlative cache of rare-earth elements—a coveted subset of so-called critical minerals that have become essential to high-tech manufacturing and yet are in short supply in the U.S. and many nations. The prized deposit is comparable to the premier site mined in China.

Geologists long had hints that Afghanistan was rife with massive, untapped stores of critical minerals worth billions or even trillions of dollars. And political leaders knew that if the volume of minerals was extractable, the wealth might allow Afghanistan's economy to transition away from its dependence on opium production, making the country more politically stable. But before any mining company will dig in, someone has to figure out whether the deposits hold enough treasure to be worth the cost. That means putting boots to dirt: collecting samples and mapping the rocks in detail. The USGS has now compiled reams of data from its dangerous forays into regions around the country. After high-level talks with Medlin about the latest information, senior officials at the U.S. Department of Defense and Department of State have become convinced that mineral riches could well help to transform Afghanistan. Indeed, a land rush of sorts has already begun. A major mining company from China has called dibs on a huge copper deposit in a $2.9-billion venture that is now Afghanistan's largest development project. U.S. interests have invested in gold. And Indian firms are the majority of almost two dozen that are clamoring for iron.

The USGS's latest assessments of the nation's mineral bounty were to be made public in a landmark report rolled out in Kabul and at the Afghan embassy in Washington, D.C., at the end of September. But as of August, when this article was being written, Medlin and other USGS scientists had already told me that the concentration and access of Afghanistan's minerals could make the country one of the most important mining centers on earth. Notably, Afghanistan could become a major supplier of rare earths as China hoards its own. How soon foreign investors will be willing to mine for those elements is unclear, however. The site examined in February lies in the southern part of the country—the most violent region, under the strongest Taliban control. Yet if mining of copper and other metals can take off in the north, that surge could create an enormous commercial and political "gold rush" that could finally help drive out the opium and Taliban strongholds, possibly creating a dramatic shift in U.S. military action and foreign policy and a blow to terrorism.

Such a prospect could never have become a serious possibility if geologists had not made extraordinary efforts to do science in a war zone—a story that has gone largely untold until now. Medlin and 50 other USGS scientists have been exploring Afghanistan for seven years and have gone to great lengths to train the country's geologists to do the same work on their own. Medlin and others will be back in Kabul in the coming months, helping Af-

Afghanistan's Promise as a Global Mining Center

An astounding variety of minerals lie buried in Afghanistan, including seven world-class deposits (*red labels*). Based on recent science, senior officials think mining could make the country economically stable and cut its heavy dependence on foreign aid and illicit opium trade. Outside nations have already invested in two sites, and six more are scheduled for auction (*key*); infrastructure will have to be improved, however. Production at a single large mine could provide jobs for tens of thousands of Afghans.

SOURCES: USGS (*base image and resource overlay information*); U.N. DEPARTMENT OF SAFETY AND SECURITY, AFGHANISTAN OPIUM SURVEY 2010, SUMMARY FINDINGS, U.N. OFFICE ON DRUGS AND CRIME (*security levels*); GOVERNMENT OF AFGHANISTAN, AFGHANISTAN OPIUM SURVEY 2010, SUMMARY FINDINGS, U.N. OFFICE ON DRUGS AND CRIME (*opium cultivation*)

Map by XNR Productions

Commercial mining is more likely to begin in northern regions, which have less risk for violence (*top right*), Taliban intrusion or opium cultivation (*bottom right*). Success in the north, however, could create strong economic and political pressure to develop the south as well.

ghan scientists to interpret the latest reports and make practical determinations about dozens of new mineral deposits. And plans are afoot to take an even deeper look at the rare-earth find, which they suspect is much larger than the initial estimate suggests.

RARE (EARTH) FINDS

FOR DECADES most assertions about Afghanistan's mineral worth were guesswork. In 2007 Medlin's team had identified the 24 most promising mining regions throughout Afghanistan's arid plains and high mountains, based on painstaking integration of unpublished field reports from the Soviet era and before. But the governments of both the U.S. and Afghanistan basically ignored the information until two years later, when Paul A. Brinkley took notice. A U.S. under secretary of defense who had overseen the Pentagon's efforts to boost business in Iraq and Afghanistan, Brinkley figured that minerals were the best bet for beating opium, and he asked Medlin for help. Medlin knew it would take much more sophisticated science to entice mining companies to bid for sites. Companies typically invest lots of money determining whether to mine a given site, and most of them would not send their own scientists into a war zone.

In 2009 Brinkley's task force called on Medlin to do just that. Since then, the USGS has used satellite imagery, remote-sensing surveys and on-the-ground fieldwork under military cover to vet old estimates and pinpoint the most promising new deposits. Medlin can now say with certainty that at least half a dozen metal deposits are equivalent to those being exploited at the most productive mines around the world.

The rocks flush with rare-earth elements are situated near the heart of a dead volcano in the dry southern plains of Helmand province, not far from the village of Khanneshin. The volcanic landscape would be tricky for a geologist to navigate on foot even without the possibility of hostile militants hiding around the next crag. USGS scientists have been motivated to risk visiting the volcano, which is well within the Red Zone, in part, by the groundswell of concern about how the world's industries will feed their ever increasing need for critical elements. China currently provides 97 percent of the world's rare-earth supply, which makes other industrial countries nervous, particularly considering its recent slashing of exports to Japan [*see box on page 64*]. Global demand for other minerals is also soaring, and prices are rising with it. A decade ago copper was about 80 cents per pound; it is now roughly $4.

Medlin's crew had tried, during two earlier marine-chaperoned visits to the volcano, to verify Soviet-era claims that rocks containing the prized metals existed there. In February the team discovered a sizable swath of rocks enriched in the so-called light rare-earth elements—including the cerium used in flat-screen TVs and the neodymium used in high-strength magnets for hybrid cars.

So far the team has mapped 1.3 million metric tons of the desirable rock in Khanneshin, holding enough rare earths to supply current world demand for 10 years. The Pentagon has estimated its value at around $7.4 billion. Another $82 billion in other critical elements may be at the site. With more time on the ground and the right kind of geophysical surveys, the scientists suspect they would discover that the rare-earth deposit could be two or three times more massive. Looking across a steep valley they did not have time to explore, the geologists say they could see what was almost certainly a continuation of the same rock formation. High-altitude imagery that measures variations in the magnetism and density of deeply buried rocks suggests the desirable material probably goes much deeper as well.

Any mining at the Khanneshin volcano would probably still be years off, however. Afghanistan has little experience with heavy industry, no real railroads and hardly any electrical power in rural areas. Those challenges are not the problem, though; major mining companies are accustomed to pioneering undeveloped frontiers in remote parts of Indonesia, Chile and Australia, for example. The need for exceptional security against hostile forces is the potential deal breaker. Coalition forces passed control of the provincial capital, Lashkar Gah, to Afghan security forces in July, making regional safety even more uncertain.

HEAVY METAL

RIGHT NOW the multibillion-dollar investments needed to open mining in Afghanistan are more palatable in the northern half of the country, where danger is less immediate, Medlin says. And that is not a bad deal. Those areas harbor untapped masses of rock containing copper, gold and iron worth hundreds of billions of dollars. Afghanistan's Ministry of Mines is keen to inspire a landgrab for those commodities. The first bite came in 2007, when China Metallurgical Group outbid four other foreign investors for a lease to develop a copper deposit known as Aynak in the mountains south of Kabul. Expecting the deposit to provide $43 billion over the life of the mine, the company agreed to build two power plants to drive mining equipment and supplement the regional power grid, as well as a portion of the railroad needed to link the mine to existing rail lines in the former Soviet republics to the north.

Further interest in the country's minerals stalled, however, until Brinkley got involved. Based on new details that Medlin's team collected, the Pentagon has reinvigorated interest by hiring a major mining-consulting firm to compile information on the most promising sites in a format attractive to foreign investors. Late last year these efforts paid off. Western investors, led by the chair of J. P. Morgan Capital Markets, injected $50 million into a small artisanal gold prospect in an alpine valley east of Mazar-e Sharif. The goal is to get a mine up and running with local labor and modern equipment by early next year.

More activity may arise soon. With the help of the Pentagon and the World Bank, Afghanistan's Ministry of Mines intends to begin auctioning off six other major mineral tracts by the end of the year. First is Afghanistan's most potentially lucrative stash: iron concentrated in Haji-Gak, mountainous terrain about 130 kilometers west of Kabul (and conveniently close to the planned railroad northward from Aynak). Estimated at a whopping $420 billion, the resource could bring in $300 million in government revenue each year and employ 30,000 people, according to the Afghan ministry. Like many of the nation's buried riches, portions of this vast deposit, which crops out in easily visible, dark black rocks, were discovered more than a century ago, but Afghanistan has never had the right combination of wherewithal, inclination and stability to start a major mining operation. Now it has taken the first step: enticing foreign investors. Bids were due in early September from the 23 international mining companies that lodged formal expressions of interest with the Afghan government late last year, including the Chinese Aynak contract winners.

Geologists Said Mirzad (*far left*) and Stephen Peters track rare-earth elements in southern Afghanistan as U.S. Marines guard against Taliban fighters. Deposits of copper (*above*) much farther west could be worth $29 billion.

COURTESY OF USGS

TAKING OVER

SUCCESSFULLY CLOSING these and other deals will require still more geology, and Afghanistan's scientists need to take charge. Bringing them up to speed on modern science and information technology was the USGS's primary goal in first entering the country (and still is). That goal motivates Medlin and a close USGS colleague, Said Mirzad, an Afghan-American geologist who visited the Haji-Gak iron deposit more than 30 years ago when he was director of the Afghanistan Geological Survey. Mirzad says he had a clear vision of trucking Haji-Gak's iron ore to Pakistan or possibly developing a local steel mill. But the 1979 Soviet invasion and subsequent occupation cut that dream short. The Soviets imprisoned Mirzad multiple times before he finally fled to the U.S. with his wife and two young sons in 1981. The country's scientific capacity stagnated in the decades of strife that ensued.

The 2001 U.S. invasion opened the door. Within three weeks of the September 11 terrorist attacks, Mirzad and Medlin received authorization—and, later, funding from the U.S. Agency for International Development—to help the Afghans firmly establish what natural resources lay buried in their native soil and to train scientists who could help advise the government about exploiting those resources. Such activities are typical work of the USGS, which has helped dozens of troubled countries rebuild their natural-resources sectors. Medlin's team knew next to nothing about the world-class potential of Afghanistan's copper and rare-earth deposits, and minerals certainly were not yet seen as a competitor to opium.

"After 25 years of war, we had no idea if there would be any geologists in Kabul when we got there," recalls Mirzad, who accompanied Medlin and seven other Americans on the first USGS visit in 2004. When they arrived at the headquarters of the Afghanistan Geological Survey, they found a bombed-out, pockmarked shell next to a slaughterhouse. There were no windows, doors, plumbing or electricity. Bullet holes studded the walls; a rocket had passed clean through the director's office. Still, roughly 100 geologists and engineers were coming into work a few hours a day, mainly to sort old reports they had hidden at home during the Taliban regime. Many of them cobbled together an income by selling cigarettes or driving taxis. Happily, their basic science training was very good. What they were missing was knowledge of the scientific and technological advances that had been developed since the early 1980s. One Afghan chemist recoiled when someone pulled out a laptop: "She wouldn't touch it, because she was afraid it would electrocute her," Medlin recalls.

Teaching the Afghan scientists the fundamental concept of plate tectonics was central. This theory—that the planet's crust is broken up, like a jigsaw puzzle, into pieces that move and crash together—revolutionized understanding of the earth in the years after the Afghans were cut off from the outside world. It explains why earthquakes occur, volcanoes erupt and mountains rise up. It also explains why Afghanistan, slightly smaller than Texas, is so unusually rife with minerals. Much of the now landlocked country formed through collisions of four or five crust pieces. These convergent boundaries tend to be where many of the world's major metal deposits occur.

One exercise the scientists hope to carry out is a detailed geophysical survey over the Khanneshin volcano. Medlin's crew, with the U.S. Naval Research Laboratory, had conducted airborne surveys from a high-flying NP-3D aircraft based on craft used for hunting down enemy submarines during the cold war. By charting the earth's magnetism and other properties, the geophysicists generated three-dimensional views of the uppermost 10 kilometers of Afghanistan's bedrock. Flown slowly and at lower altitude, the same instruments could discern far greater detail, revealing how specific mineral deposits extend down into the ground. The $7.4-billion estimate for the rare earths there assumes, very conservatively, that the rock is only 100 meters thick. It could easily be thicker. Medlin had hoped to do that survey, but the security clearance never came—too much risk of the plane being shot down, he assumes. So he convinced Brinkley to buy the Afghanistan Geological Survey the same instruments that can be carried on foot, and Medlin is bringing Afghan geologists to the U.S. to learn how to use them.

Medlin and Mirzad are both pleased with a $6.5-million renovation of the Afghanistan Geological Survey headquarters building in Kabul, which has left it looking as good as its American counterpart in northern Virginia, Mirzad says. "And the cafeteria is better," he adds with a wink. The Afghan agency now houses a

state-of-the-art digital data center and employs 100 full-time scientists and engineers who are conducting mineral-assessment surveys on their own. The Afghans' recent fieldwork at a copper deposit near Dusar-Shaida is the main reason it is included among those scheduled for upcoming bidding, Medlin says.

FORMIDABLE CHALLENGES

THE ADVANCING SCIENCE makes it clear that lucrative mining is finally possible in Afghanistan, and for the first time major investors are poised to commit. A national economy driven by mining could end opium's dominance and help to stabilize the country, which would give the U.S. and other nations good reason to scale back their heavy military involvement there.

Even so, some Afghans worry about whether mining would be good for the nation's people. Major mineral exploitation in some poor countries has been more curse than blessing. The discovery of oil in Nigeria more than 50 years ago has earned billions of dollars for petroleum companies and the government, but most Nigerians still live on less than $1 a day. Development could fuel Taliban resurgence and government corruption. Medlin promotes an "absolute imperative for transparency" as one safeguard; all the raw data the USGS has so carefully compiled are owned by the Afghan government, which permits the U.S. government to make the information available on the Internet.

Environmental protection is another concern. In many parts of the world where massive open-pit mining operations exist, authorities face decades of accumulated contaminants that must be cleaned up. Standard procedures for extracting rare-earth elements, for example, leave rubble strewn with uranium and other radioactive debris that threaten health. Transforming Afghanistan into one of the world's major mining centers without similar consequences will require serious forethought and accountability.

These challenges, and final determinations about which specific deposits are worth mining, are expected to fall mainly to Afghan scientists from now on. The USGS's Pentagon funding runs out at the start of the new fiscal year in October, and without military protection fieldwork for USGS scientists will be next to impossible. Native Afghan scientists travel more freely, so Medlin's team will do its best to advise them as they generate more detailed information. To keep up the momentum, Medlin has secured $8.7 million from USAID to continue processing the satellite imagery and other remote-sensing data the USGS has already collected to spot more promising deposits. "It's basically like picking out a dime in a million pennies," Medlin says. "We're seeing mineral-deposit anomalies that the Soviets and Afghans never knew existed."

Whether newly trained scientists and politicians can follow through with business development is unclear. Luckily, the rocks can wait. They have all the time in the world. ■

MORE TO EXPLORE

Afghanistan Geological Survey: www.bgs.ac.uk/afghanminerals

Afghanistan's Ministry of Mines: http://mom.gov.af/en

U.S. Task Force for Business and Stability Operations: http://tfbso.defense.gov

USGS Projects in Afghanistan: http://afghanistan.cr.usgs.gov

SCIENTIFIC AMERICAN ONLINE
For a discussion about mining complications and a slide show on exploration, see ScientificAmerican.com/oct2011/afghanistan

Global Demand Stresses Limited Supply

By Mark Fischetti, staff editor

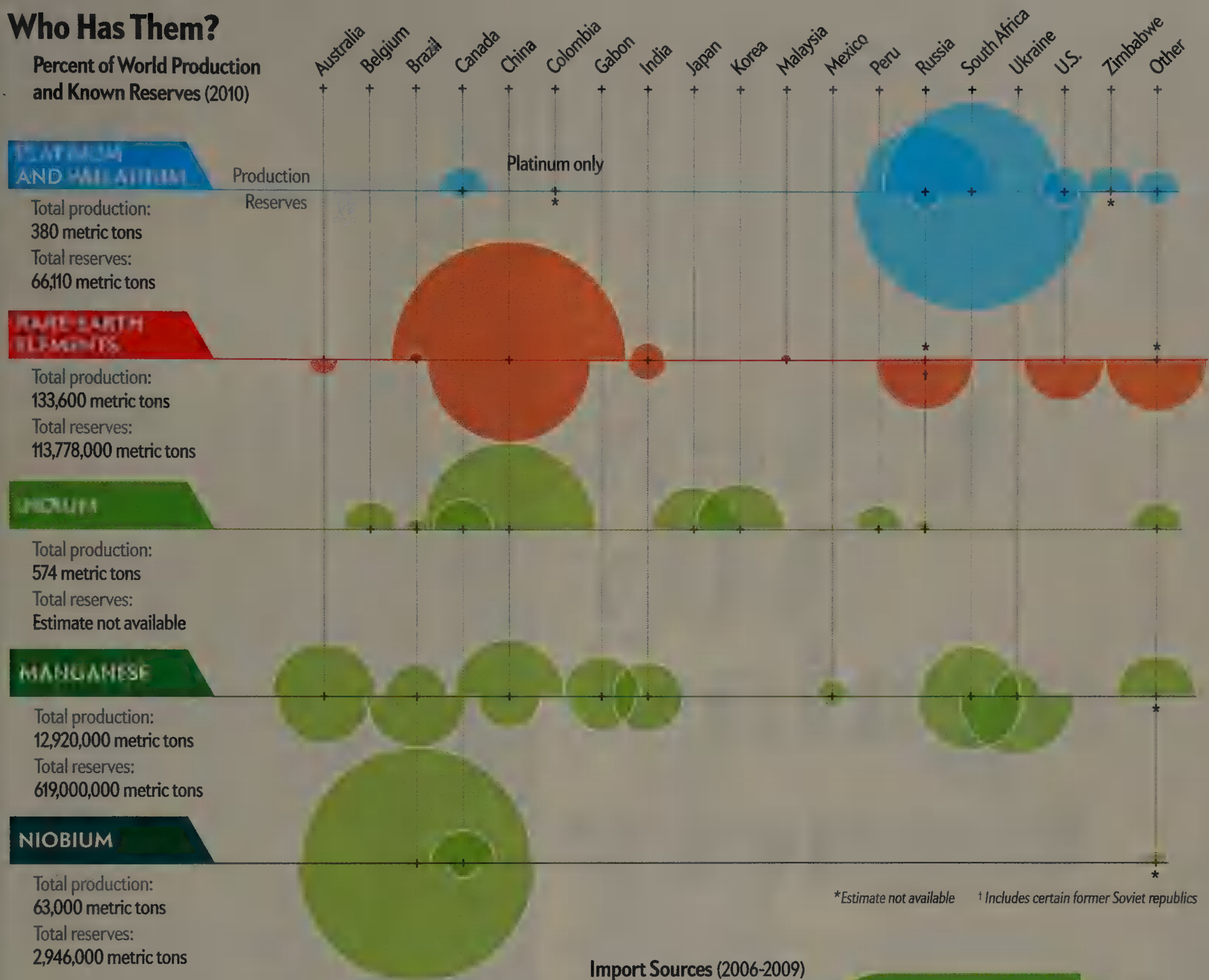
A mere few countries control worldwide production of many minerals that have become essential to high-tech manufacturing: europium for TV displays, neodymium for computer disk drives. And some countries, such as China, have begun hoarding the resources for their own companies.

As a result, industrial nations are becoming increasingly tense about their sources of "critical elements"—minerals that are crucial but whose supply could be restricted. Most critical for the U.S. are the six elements in the platinum group of metals, the 17 elements known as rare-earth elements, as well as indium, manganese and niobium, according to the U.S. Geological Survey. Which nations have them (*top right*), and how dependent the U.S. is (*bottom right*), could affect the American economy and national security (in the case of military products) if trade is curtailed or new deposits are not found. More mapping is needed to determine the impact of Afghanistan's potentially vast resources.

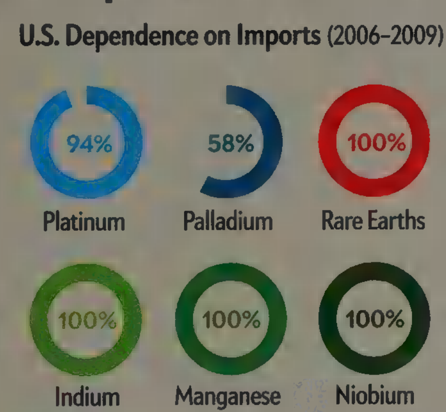
What Are They Used For?

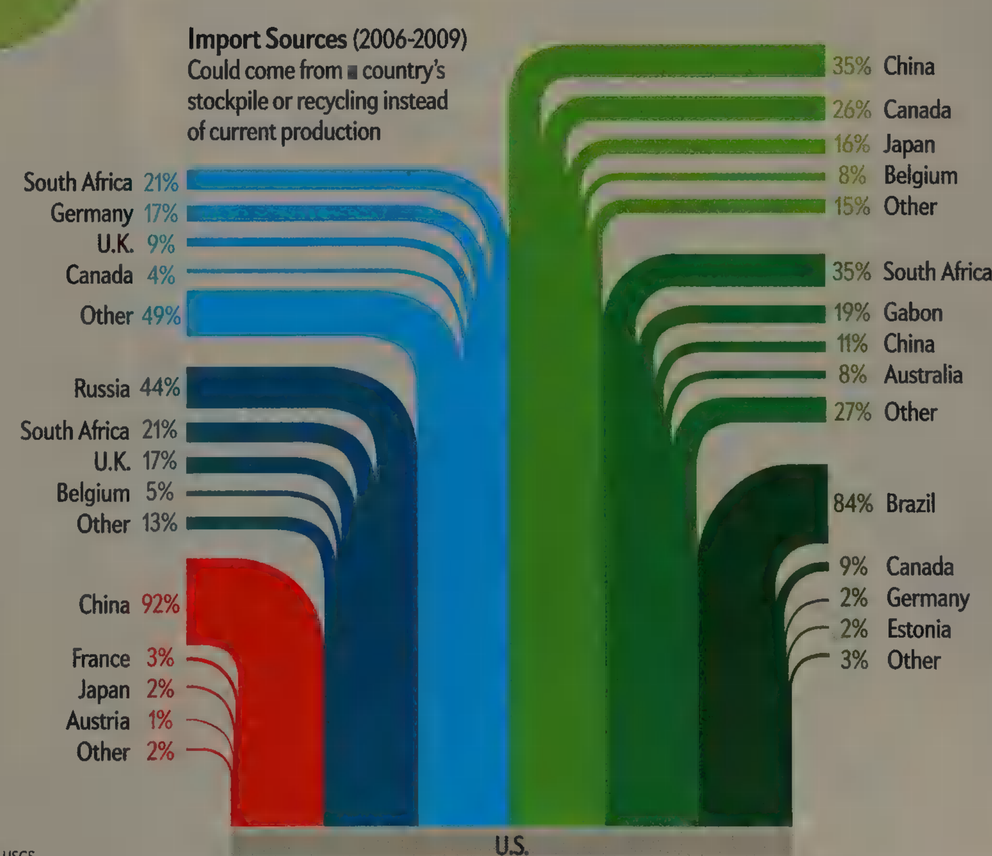
PLATINUM GROUP METALS	
Platinum	Catalytic converters, electronics, chemical processing
Palladium	Catalytic converters, capacitors, carbon monoxide sensors
Rhodium	Catalytic converters, chemical processing
Ruthenium	Electronic contacts and resistors, superalloys
Iridium	Spark plugs, alloys, chemical processing
Osmium	Electronic contacts, electron microscopy, surgical implants
RARE-EARTH ELEMENTS	
Scandium	Aerospace components, aluminum alloys
Yttrium	Lasers, TV and computer displays, microwave filters
Lanthanum	Oil refining, hybrid-car batteries, camera lenses
Cerium	Catalytic converters, oil refining, glass-lens production
Praseodymium	Aircraft engines, carbon arc lights
Neodymium	Computer hard drives, cell phones, high-power magnets
Promethium	Portable x-ray machines, nuclear batteries
Samarium	High-power magnets, ethanol, PCB cleansers
Europium	TV and computer displays, lasers, optical electronics
Gadolinium	Cancer therapy, MRI contrast agent
Terbium	Solid-state electronics, sonar systems
Dysprosium	Lasers, nuclear-reactor control rods, high-power magnets
Holmium	High-power magnets, lasers
Erbium	Fiber optics, nuclear-reactor control rods
Thulium	X-ray machines, superconductors
Ytterbium	Portable x-ray machines, lasers
Lutetium	Chemical processing, LED lightbulbs
OTHER CRITICAL MINERALS	
Indium	Liquid-crystal displays, semiconductors, solar thin films
Manganese	Iron and steel production, aluminum alloys
Niobium	Steel production, aerospace alloys

Who Has Them?



How Dependent Is the U.S.?





What on earth can the U.S. do? China produces about 97 percent of the world's rare-earth oxides. The overwhelming U.S. source, the Mountain Pass mine in California, was closed in 2002. Molycorp Minerals will reestablish volume production there in 2012, but neither Molycorp nor other U.S. companies will have the facilities needed to refine the oxides into useful products; rebuilding that supply chain could take up to 15 years, according to the U.S. Government Accountability Office.

SOURCE: MINERAL COMMODITY SUMMARIES 2011, U.S. DEPARTMENT OF THE INTERIOR AND USGS

Graphic by Jen Christiansen

Eric von Hofe has spent his career in biotechnology, investigating novel cancer therapies. He is president of Antigen Express in Worcester, Mass.

MEDICINE

A New Ally against Cancer

The FDA recently okayed the first therapeutic cancer vaccine, and other drugs that enlist the immune system against tumors are under study

By Eric von Hofe

FOR DECADES CANCER SPECIALISTS HAVE OFFERED PATIENTS THREE main therapies: surgery, chemotherapy and radiation. (Some cancer survivors pointedly refer to this harsh trinity as "slash, poison and burn.") Over the years continual refinements in these admittedly blunt instruments have made the more severe side effects increasingly manageable. At the same time, effectiveness has improved markedly. And new, very targeted drugs (Herceptin and Gleevec) have become available for a few specific cancers. All told, the average five-year survival rate for invasive cancers as a group has risen from 50 percent to 66 percent in the past 30-plus years. In spite of these gains, many cancer survivors will not have a normal life span.

Photograph by Dan Saelinger

Researchers have long suspected that they could add a weapon that would dramatically increase cancer survival rates without producing serious side effects if they could just figure out how to prod the body's own immune system to do a better job of fighting malignancies. But decades of effort met with one failure after another. In the 1980s, for instance, overheated hopes that an immune system molecule called interferon would rouse the body's defenses to cure all or most cancers were dashed after a few more years of research. Today interferon has a place but is not the cure-all once envisioned. By the first decade of this century a great number of clinical trials were being conducted using lots of different types of vaccine-related approaches, but nothing seemed to be working. It was starting to look as though the long-hoped-for general weapon against a broad range of tumors would never materialize.

It still has not. But something happened in the summer of 2010 suggesting that the age of false starts and blind alleys in the effort to awaken the immune system may finally be drawing to a close: the U.S. Food and Drug Administration approved the first vaccine to treat a cancer. The drug, called Provenge, is not a cure, but it—along with standard chemotherapy—already has given hundreds of men with advanced prostate cancer a few extra months of life.

This positive turn of events occurred after scientists reexamined a few fundamental assumptions about how the immune system works against cancer cells as well as how tumors fight back against immunological attacks. Today cancer researchers are cautiously optimistic that we can develop additional, very specific immune-boosting therapies that can be used routinely alongside surgery, chemotherapy and radiation to subdue cancer while triggering side effects that are no worse than a bad cold.

A NEW ALLY

MANY OF US are focusing particularly on therapeutic cancer vaccines. Unlike most familiar vaccines, which prevent certain infections that can lead to brain damage (measles), paralysis (polio) or liver cancer (hepatitis B) from taking hold in the first place, therapeutic cancer vaccines train the body to recognize and destroy cancer cells that already exist within its tissues and to keep killing those malignant cells long after treatment has ended.

Developing such vaccines is easier said than done. Most preventive vaccines trigger a simple antibody response, which is usually pretty good for protecting against lots of different kinds of infections. The antibodies just stick to flu viruses, for example, and stop them from infecting cells. In general, however, antibody responses are not strong enough to kill cancer cells. For that kind of job, the immune system needs to stimulate a group of cells called T cells. There are two main types of T cells in the body. Scientists often distinguish between different kinds by referring to various distinctive proteins, termed receptors—such as CD4 or CD8—that sit on their outer membranes. The kinds of T cells that are especially good at directly destroying malignant cells—assuming they can be induced to recognize the cancer cells as dangerous—display CD8 receptors. (These T cells are called CD8+ cells because the CD8 receptor is present.)

Despite these complexities, creating a cancer vaccine is not a new idea. In the waning years of the 19th century, long before anyone had ever heard of a CD8+ cell, William B. Coley started injecting cancer patients with a substance that came to be called Coley's toxin. An orthopedic surgeon at what is now Memorial Sloan-Kettering Cancer Center in New York City, Coley was intrigued by reports of cancer patients who apparently had been cured of their disease after a brief bout with a life-threatening infection. In an attempt to simulate the infection without risking its potentially deadly consequences, Coley prepared a solution that mixed two strains of deadly bacteria. He gently heated the preparation so that the bacteria were killed and rendered harmless. Enough of the bacterial proteins remained in the brew, however, that the patients' bodies responded by generating very high fevers.

Coley hypothesized that high fevers could jump-start his patients' moribund immune systems into recognizing and attacking the abnormal growths within their bodies. He extended the length of his patients' artificial fevers with daily injections of increasingly concentrated dead bacteria. Remarkably, long-term survival was greater among the cancer patients who received the toxin than among those who had not. Coley argued, with some justification, that his toxin had served as a kind of vaccine against cancer.

By the 1950s, however, physicians started getting more consistent results with chemotherapy. As Coley's bacterial toxins fell out of favor, the whole notion of creating vaccines to treat cancer ground to a halt.

But study of the immune system and its possible role in cancer did not stand still. Gradually researchers developed evidence to support the idea, first suggested by Paul Ehrlich in 1909, that the immune system continually surveys and destroys newly arisen cancer cells. This so-called immune surveillance theory gained further credibility in the 1980s, when investigators calculated that the high level of spontaneous mutation in human cells that they

IN BRIEF

Conventional treatments for cancer—surgery, chemotherapy and radiation—have increased survival rates since the 1970s, but many survivors still do not achieve a normal life span.

Researchers believe the results would be better if they could recruit a new ally against malignancy: the body's own immune system.

Over the past decade several attempts to boost the immune response artificially—through vaccination or other drug development—have failed.

But the tide seems to be changing. A cancer vaccine for treating prostate cancer has been approved, and a new generation of therapeutic cancer vaccines is now being tested.

PERSEVERANCE

The Long March

Boosting the immune system's cancer-fighting ability has taken decades of research.

1890s
William B. Coley stimulates the immune systems of cancer patients by injecting them with mixtures of dead bacteria.

1909
Paul Ehrlich suggests that the immune system may suppress tumor development.

1975
Monoclonal antibodies are created, allowing development of highly specific immunological tools.

AP PHOTO

were observing should have resulted in many more malignant growths than were indeed detected. Somehow the body was regularly finding and destroying numerous cancerous cells on its own.

Even after the occasional tumor managed to avoid eradication, the evidence suggested, the immune system kept fighting—just not as effectively. Pathologists had long noted that tumors were frequently infiltrated by immune cells, giving rise to the concept that tumors were "wounds that would not heal." In addition, further experiments showed that as a tumor grows, it releases more and more substances that actively suppress T cells. The question now became how to design cancer vaccines that would tip the balance in favor of T cells able to eradicate the tumor.

An answer began to emerge in 2002, when a team of scientists at the National Cancer Institute (NCI) showed that another immune T cell, known as a CD4+ cell, was a critical component of an effective anticancer response. CD4+ cells are sort of like the generals of the immune system: they give the orders about who and what to attack to the foot soldiers—which, in this scenario, are the CD8+ cells—that do the actual killing. The NCI team, led by Steven Rosenberg, took T cells out of 13 advanced melanoma patients whose tumors had metastasized, or spread, throughout their body. The researchers selectively activated the removed immune cells to target and attack the melanoma cells in a test tube. Then the scientists grew the activated cells in large amounts and infused them back into the patient. The NCI team's approach, referred to as adoptive immunotherapy, is, in effect, a kind of self-transplantation of immune cells (altered artificially outside the body) and, as such, differs from vaccination, which causes the immune system to generate its own targeted immune cells inside the body.

Previous adoptive immunotherapy treatments using just CD8+ cells had shown no benefit. But when the NCI team added CD4+ cells to the mix, the results were remarkable. Tumors shrank dramatically in six subjects, and blood tests from two of the six showed that they were still making powerful anticancer immune cells on their own more than nine months after the treatment had ended. For the most part, patients experienced temporary flu-like symptoms as a result of the treatment, although four of them also suffered a complex autoimmune reaction that led to the loss of pigment from parts of their skin.

The NCI results offered a convincing proof of concept: an immune response based on T cells could, in fact, be boosted precisely enough to destroy tumors. The number of cloned immune cells needed per patient in this experiment was staggering: more than 70 billion CD8+ cells and CD4+ cells—or several hundred milliliters in volume. But at least the scientific community now believed that immunotherapy against cancer could work. The next steps were to figure out how to obtain the same result in a simpler fashion—that is, without having to remove cells from the body, grow them in great numbers and reinfuse them later. In other words, it should be possible to make the body grow most of the additional cells it needed on its own—which is exactly what it does in response to an effective vaccine.

MULTIPLE STRATEGIES

MY COLLEAGUES AND I at Antigen Express were gratified when Rosenberg's group showed that a cancer vaccine would have to elicit both CD4+ and CD8+ cells to be effective. We had previously argued the same point based on animal studies and had essentially staked the future of our company on that belief.

Basically, there are three elements to making a cancer vaccine. The first is to decide precisely what molecular feature, or antigen, in a malignant tumor the immune system should recognize as foreign and target for killing. The second is to decide how to deliver a triggering agent (or vaccine) to the immune system that ramps it up to attack cancer cells. And the third is to decide which cancer patients to treat and when during the course of their disease to administer the vaccine.

Over the past several years researchers in the biotech industry have considered a wide range of proteins, as well as pieces of proteins (called peptides), as the potential starting points for driving an immune response robust enough to kill cancer cells. (Other possibilities for priming the pump include using bits of genetic material that encode cancer proteins or even whole cancer cells after they have been irradiated.) It turns out that the genetic alterations that allow cancer cells to grow uncontrollably also cause them to make some proteins in much higher amounts than are found anywhere else in the body. About 10 companies, including our own, have selected various examples of these peptides to fulfill the first two requirements for making a cancer vaccine: the starting point and the delivery mechanism.

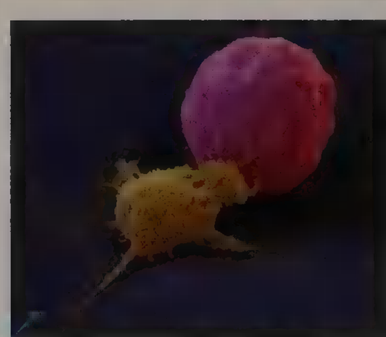
Part of what makes peptide vaccines particularly attractive is

1980
Researchers insert a gene that codes for interferon into bacteria, allowing the immune-stimulating molecule to be mass-produced for the first time.

1986
The Food and Drug Administration okays interferon, the first proved immunotherapy against cancer, for the treatment of hairy cell leukemia.

1997
The FDA approves the first monoclonal antibody treatment against cancer, with the brand name Rituxan, for non-Hodgkin's lymphoma.

1998
The FDA approves the monoclonal antibody Herceptin for the treatment of metastatic breast cancer.



2002
Researchers at the National Cancer Institute prove that a T cell-based treatment against cancer is possible and requires the contribution of two kinds of immune cell: CD8+ T cells (*gold, seen at left attacking cancer cell*) and CD4+ T cells.

2010
The FDA approves Provenge, the first vaccine meant to elicit an attack on an existing tumor, for advanced prostate cancer.

GARY RETHERFORD *Photo Researchers, Inc.* (*left*); PHOTO RESEARCHERS, INC. (*right*)

that these bits of protein are small in size, inexpensive to synthesize and very easy to manipulate, which means that they can be readily formulated into a vaccine that is simple to manufacture in large amounts. Furthermore, since the peptides that have been identified show up in many people with different types of cancer, they can be used in formulations that would help many people without doctors having to compose individual vaccines for each person, which they have to do with cell-based immunotherapies. Finally, all the peptide vaccines tested so far produce relatively mild side effects, such as temporary irritation at the injection site and perhaps a fever or other flulike symptom.

Ten years ago scientists at Antigen Express made a few key modifications to a peptide that had been used in an experimental vaccine against breast cancer. Known as HER2, this particular protein is also the target of Herceptin, a monoclonal antibody treatment against certain types of breast cancer. Our researchers found that adding just four more amino acids to the peptide dramatically increased its ability to stimulate CD4+ cells, as well as CD8+ cells, against breast cancer cells that make the HER2 protein. This finding was the innovation on which we bet the company's future. Preliminary data published earlier this year from an independent study that compared our HER2-enhanced vaccine against two other peptide vaccines designed to stimulate only CD8+ cells suggests that we are on the right track.

Some companies, such as Dendreon, makers of the newly FDA-approved Provenge, placed their bets differently. Dendreon and some other companies are providing targets specific for cancer cells directly to an immune cell known as a dendritic cell. Scattered throughout the body, particularly in tissues that come into contact with the outside world (such as the skin or the lining of the digestive tract), dendritic cells act like the immune system's sentinels and are among the first defenders to alert the T cells that something is wrong. Because immune cells take orders only from other immune cells that are genetically identical to them, however, the necessary dendritic cells must be harvested from each individual patient, loaded with the cancer-specific protein and then reinfused back into the patient—all at a cost of about $93,000 for a full course of treatment. Side effects include chills, fever, headache and, less commonly, stroke. But a short-term clinical study proved that people with advanced prostate cancer who were treated with Provenge lived, on average, at least four months longer than their untreated counterparts.

NEXT STEPS

THE FDA'S APPROVAL of Dendreon's Provenge plus promising preliminary data from clinical trials conducted by various companies, including our own, suggests that we are entering a new era in the development of cancer vaccines. As scientists venture further in this promising new endeavor, however, we are discovering that we cannot use the same yardsticks for measuring progress against cancer with immunotherapy as we do for chemotherapy or radiation. The latter two show their benefits rather quickly—within a few weeks the tumors either shrink in size, which is good, or they do not, which is bad. But data from several clinical trials suggest that it may take up to a year after treatment with a cancer vaccine for the immune system to really start making substantial progress against tumor growth.

This lag time is not entirely surprising, because the immune system needs a good deal of coaxing to attack cells that look awfully similar to normal cells in the body, as opposed to a bacterium or virus. Breaking tolerance—or the immune system's reluctance to attack cells that have arisen from the host—is perhaps the biggest obstacle in generating effective therapeutic vaccines to fight cancer. Another surprise is that tumors may actually appear to grow in size after treatment with cancer vaccines. Analysis of tumor tissue, however, shows that this increase can be the result of invading immune cells, not of tumor cell replication.

The deliberate pace with which the immune system so far seems to respond to the therapeutic cancer vaccines being developed, however, suggests two important intermediate conclusions. One, individual cancer vaccines will probably be most effective in the near term in people at earlier stages of their disease, when their tumors are not big enough to depress their immune system and they have enough time to wait for a more powerful immune response to kick in. Two, people with advanced disease probably will usually need to have their tumors shrunk through conventional treatment before they can benefit from receiving a cancer vaccine. Starting with a small tumor or shrinking existing ones are important because large, long-lived tumors are just that much better than smaller, younger ones at suppressing or evading the immune system. They have more cells that can release greater amounts and types of immune-suppressing chemicals. Late-stage cancer patients may simply have too much cancer present for even a healthy immune system to dispatch.

In spite of these obstacles and complexities, the signs are clear: a patient's own immune system can be effectively enlisted to help combat cancer. This realization has given tremendous encouragement to investigators in academia and industry who have persevered in the face of so many failures. Previous clinical trials that had been written off as failures are being reexamined to see if perhaps evidence of immune-related responses may have been overlooked. Indeed, one such trial of a potential prostate cancer vaccine (Prostvac) showed that while the compound failed to meet its original predetermined end point—lack of tumor growth—it boosted overall survival. Of course, this discovery came after the small biotech company that developed Prostvac had already gone out of business for having failed to meet the primary end point of the trial. Fortunately, another company secured the rights to develop the drug.

As for the survivors in the industry, we have been conditioned by years of frustrating results to look beyond setbacks and not to make too many promises. But the evidence from the research and clinical trials over the past couple of years leads a growing number of investigators to believe that therapeutic cancer vaccines will take a prominent role alongside surgery, chemotherapy and radiation over the next decade as an effective treatment for some of the most common cancers that plague humanity. ■

MORE TO EXPLORE

A Malignant Flame. Gary Stix in *Scientific American*, Vol. 297, No. 1, pages 60–67; July 2007.

Strategies for Cancer Vaccine Development. Matteo Vergati et al. in *Journal of Biomedicine and Biotechnology*, Vol. 2010. Published online 2010. www.hindawi.com/journals/jbb/2010/596432

A New Era in Anticancer Peptide Vaccines. Sonia Perez et al. in *Cancer*, Vol. 116, No. 9, pages 2071–2080; May 1, 2010. www.ncbi.nlm.nih.gov/pubmed/20187092

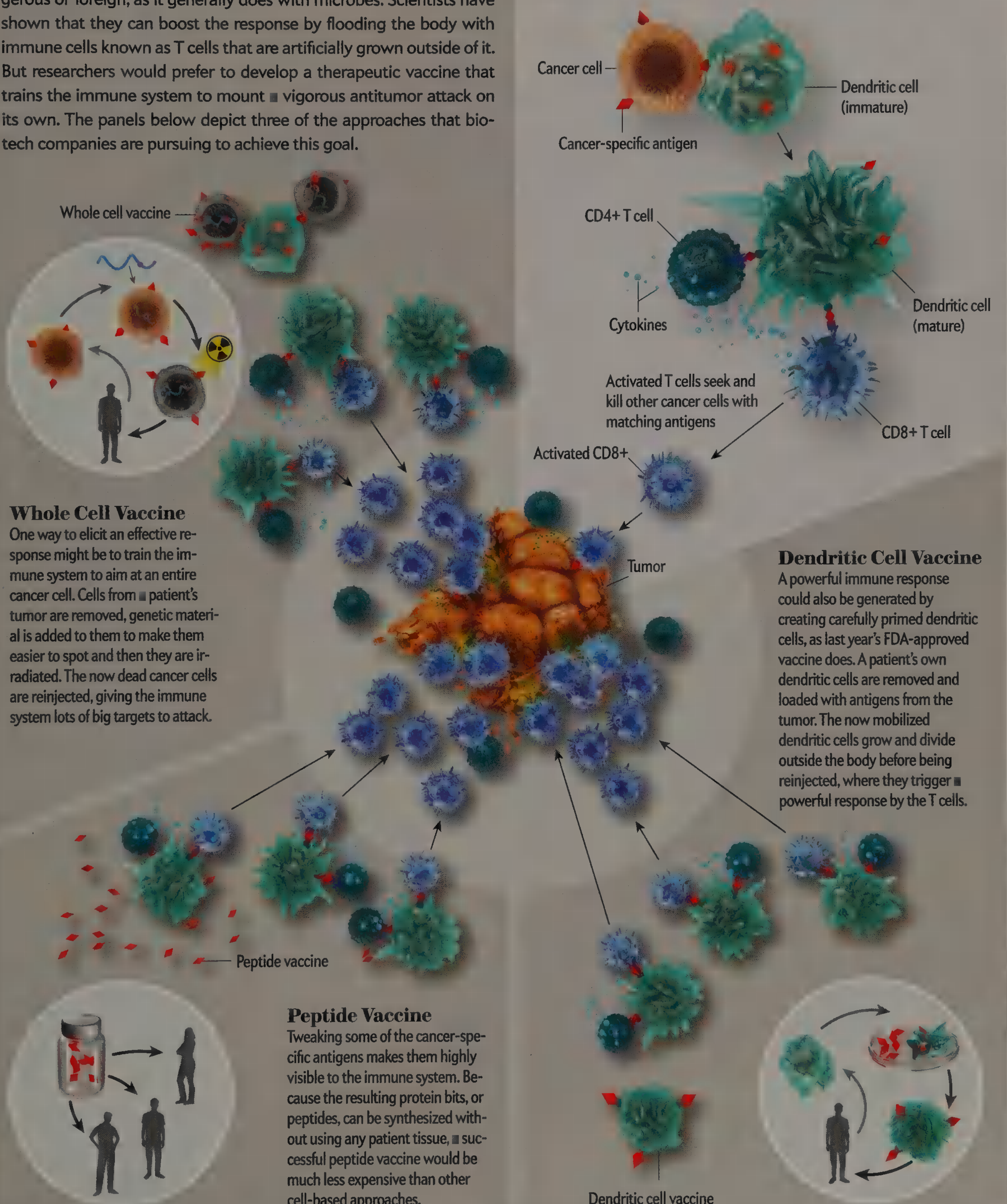
SCIENTIFIC AMERICAN ONLINE
Listen to Eric von Hofe talk about the future of therapeutic cancer vaccines at ScientificAmerican.com/oct2011/cancervaccine-podcast

Three Therapeutic Vaccine Strategies

The immune system does not easily recognize cancer cells as dangerous or foreign, as it generally does with microbes. Scientists have shown that they can boost the response by flooding the body with immune cells known as T cells that are artificially grown outside of it. But researchers would prefer to develop a therapeutic vaccine that trains the immune system to mount ■ vigorous antitumor attack on its own. The panels below depict three of the approaches that biotech companies are pursuing to achieve this goal.

Basic Cellular Immune Response to Cancer

An immune cell called a dendritic cell ingests a tumor cell and then presents substances called antigens (*red*) from the tumor to two other immune cells, the CD8+ and CD4+ T cells. The CD4+ cell releases cytokine molecules that help to activate the CD8+ cell, prompting it to attack other cells with the same antigen. Alas, the response is not always strong enough to destroy an entire tumor.



Whole Cell Vaccine

One way to elicit an effective response might be to train the immune system to aim at an entire cancer cell. Cells from ■ patient's tumor are removed, genetic material is added to them to make them easier to spot and then they are irradiated. The now dead cancer cells are reinjected, giving the immune system lots of big targets to attack.

Dendritic Cell Vaccine

A powerful immune response could also be generated by creating carefully primed dendritic cells, as last year's FDA-approved vaccine does. A patient's own dendritic cells are removed and loaded with antigens from the tumor. The now mobilized dendritic cells grow and divide outside the body before being reinjected, where they trigger ■ powerful response by the T cells.

Peptide Vaccine

Tweaking some of the cancer-specific antigens makes them highly visible to the immune system. Because the resulting protein bits, or peptides, can be synthesized without using any patient tissue, ■ successful peptide vaccine would be much less expensive than other cell-based approaches.

Illustration by AXS Biomedical Animation Studio

FORENSICS

How Skulls Speak

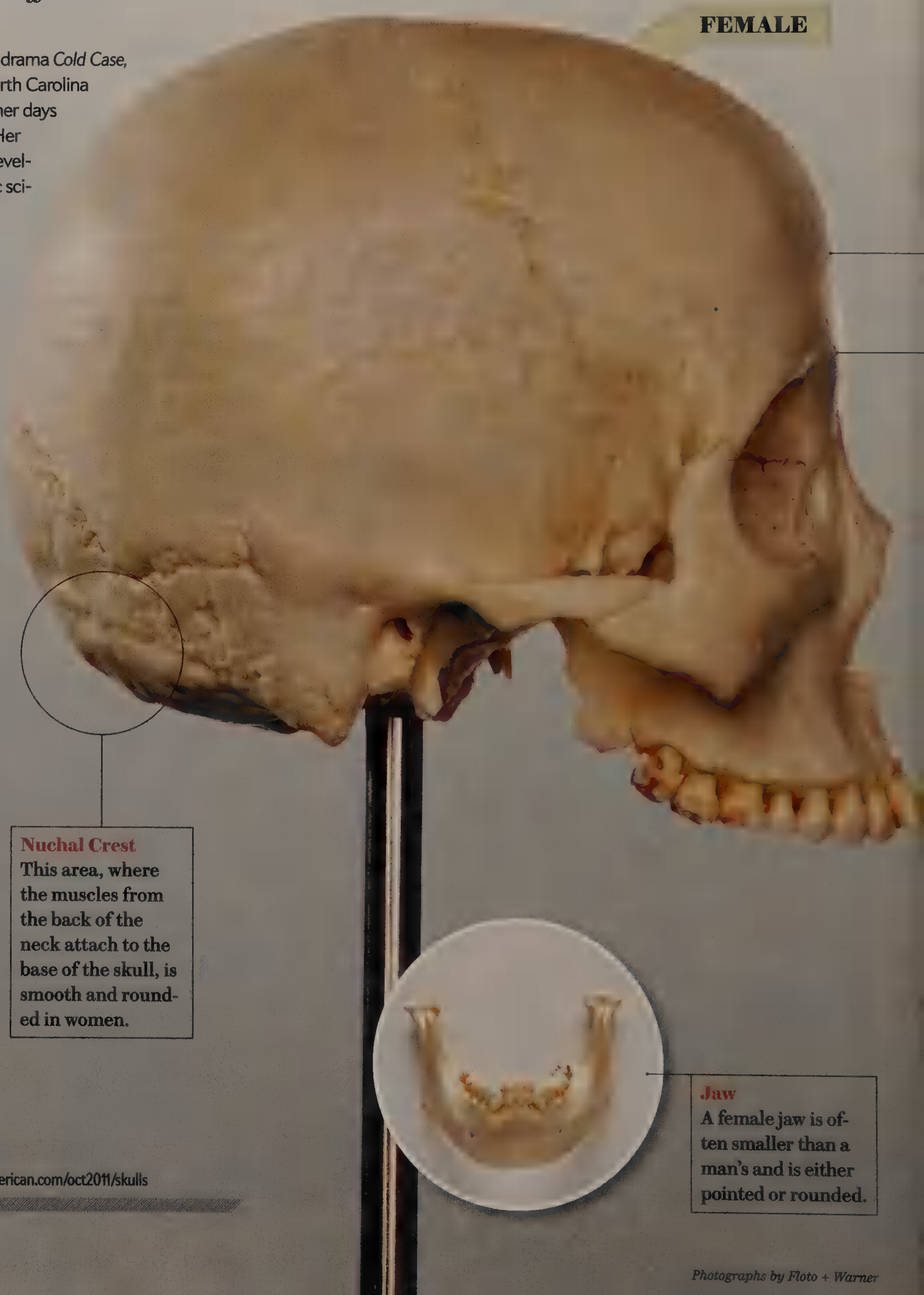
New 3-D software is helping scientists identify the sex and ancestral origins of human remains with greater speed and precision

By Anna Kuchment, staff editor

LIKE THE DETECTIVES on the CBS drama *Cold Case,* anthropologist Ann H. Ross of North Carolina State University spends many of her days thinking about unsolved crimes. Her most recent work has aimed at developing software that helps forensic scientists determine the sex and ancestry of modern human skulls.

Typically forensic scientists measure remains with sliding rulers called calipers. Doing so results in two-dimensional measurements. Ross's software, called 3D-ID and developed with a grant from the U.S. Department of Justice, relies on three-dimensional measurements that scientists take with a digitizer—a computer and stylus. "The stylus allows you to place the coordinates in real space, so you get a better idea of the actual biological form of whatever you're measuring," Ross says.

In a paper published earlier this year Ross and her colleagues found that women's skulls had grown closer in size to male skulls since the 16th century in a Spanish sample—a finding that likely translates to other population groups. Unlike older forensic software, 3D-ID lets scientists remove the size component in their analysis and look only at shape for a more accurate reading. The photographs at the right show some of the features that 3D-ID uses to determine if a skull belongs to a man or a woman. ■



Nuchal Crest
This area, where the muscles from the back of the neck attach to the base of the skull, is smooth and rounded in women.

Jaw
A female jaw is often smaller than a man's and is either pointed or rounded.

SCIENTIFIC AMERICAN ONLINE
More images and a quiz at ScientificAmerican.com/oct2011/skulls

Photographs by Floto + Warner

Forehead
Women's foreheads are more vertical than men's, which gives them a child-like appearance, Ross says. Men tend to have sloping foreheads.

Nuchal Crest
Because males have thicker neck muscles than females—and are generally more muscle-marked—this area is more prominent. It is typically rugged and has a hook.

Brow
An area called the supraorbital margin, which is just above the eye and roughly follows the brow line, is thin and pointy in women. "If you place your thumb below the outer edge of a woman's eyebrow, you'll feel that it's sharp," Ross says. Women also have either a small or nonexistent brow ridge. Men, in contrast, have a rounded supraorbital margin, and their brow ridge is more pronounced than women's.

Jaw
Males typically have a broad, square jaw.

PHYSICS

WAITING FOR

Even as the last protons spin through the most successful particle accelerator in history, physicists hope to conjure one final triumph

By Tim Folger

THE HIGGS

Night falls: The Tevatron particle accelerator outside Chicago was for 27 years the world's most powerful window into the subatomic universe.

Tim Folger is an award-winning science writer and the series editor of *The Best American Science and Nature Writing*, an annual anthology published by Houghton Mifflin.

UNDERNEATH A RELICT PATCH OF ILLINOIS PRAIRIE, COMPLETE WITH A SMALL HERD OF GRAZing buffalo, protons and antiprotons whiz along in opposite paths around a four-mile-long tunnel. And every second, hundreds of thousands of them slam together in a burst of obscure particles. It's another day at the Tevatron, a particle accelerator embedded in the verdant grounds of the 6,800-acre Fermi National Accelerator Laboratory complex in Batavia, about 50 miles due west of Chicago. There have been many days like this one, some routine, some spectacular; of the 17 fundamental particles that physicists believe constitute all the ordinary matter and energy in the universe, three were discovered here. But there won't be many more such days. By October 1 the power supplies for more than 1,000 liquid-helium-cooled superconducting magnets will have been turned off forever, the last feeble stream of particles absorbed by a metal target, ending the 28-year run of what was until recently the most powerful particle accelerator in the world.

For several hundred physicists here who have spent nearly two decades searching for a hypothetical particle called the Higgs boson, the closure means ceding the hunt—and possible Nobel glory—to their archrival, the Large Hadron Collider, a newer, more powerful accelerator at CERN on the Swiss-French border. With its 17-mile circumference and higher energies, the LHC has displaced the Tevatron as the world's premier particle physics research instrument, a position it will retain well into the next decade.

The U.S. Department of Energy's decision to shut down the Tevatron at the close of this fiscal year did not surprise anyone at Fermilab. Some physicists had recommended that the DOE fund the aging accelerator for another three years, giving it a final crack at finding the elusive Higgs, a particle that theorists believe is responsible for endowing all other particles with mass. But even the most ardent Tevatron veterans admit that the old machine has finally been made redundant. "I don't have sadness," says Dmitri Denisov. "It's like your old car. The whole history of science is one of new tools. This one lasted for more than 25 years. It's time to move on."

That can't be an easy admission for Denisov, the co-spokesperson for the team that runs D-Zero, one of two hulking detectors that straddle the Tevatron. Two years ago, during a press conference at the annual meeting of the American Association for the Advancement of Science, Denisov said, "We now have a very, very good chance that we will see hints of the Higgs before the LHC will." At the time, an electrical failure had closed the LHC for several months, and Denisov's confidence was shared by many at Fermilab. But it was not to be. When the LHC came back online in November 2009, it quickly ramped up to energies three times higher than the Tevatron could match.

For the past three decades D-Zero's main competition has been the Tevatron's other enormous detector, the Collider Detector at Fermilab, or CDF, which sits atop the accelerator a grassy mile away from D-Zero. Hundreds of physicists from dozens of countries work at each.

This past spring physicists at the CDF announced that they had found hints in their data of what appeared to be a new particle. Might the Tevatron, in its waning days, have found the first telltale signs of the Higgs? Denisov and his colleagues at D-Zero immediately began to double-check the CDF results. As SCIENTIFIC AMERICAN went to press, the issue remained unsettled. Yet one thing is clear: the intra-accelerator competition is not yet over.

IN BRIEF

The Tevatron, formerly the world's most powerful particle collider, will cease operations by October 1. It has been supplanted by the Large Hadron Collider.

Despite the shutdown, physicists at the facility are poring over data that might reveal evidence of the long-sought Higgs boson.

Scientists at Fermilab hope to build a new accelerator called Project X by 2020 and, after that, a successor to the LHC.

COURTESY OF FERMILAB (*preceding pages*)

"I want to beat Dmitri, and vice versa," says Rob Roser, leader of the CDF team. "We're cordial; we talk; we're friends. But we always wanted to beat each other. Now the endgame is different. The LHC is the bad guy. It used to be Dmitri. I never wanted the LHC to beat either one of us. It's like, you can't beat up my little brother—only I can."

With old rivalries ending (almost) and new projects just starting, Fermilab is passing through an uncertain period. The same could be said for the entire discipline of particle physics. Physicists have been waiting a very long time for a machine that might give them access to some new realm of physical reality. Given that the LHC is expected to double its collision energies within the next two years, there is no shortage of ideas about what it might discover: extra dimensions, supersymmetry (the idea that every known particle has a so-called supersymmetric twin), the Higgs, of course. Best of all would be something completely unexpected. There is another possibility, however, usually dismissed but impossible to discount. And it simultaneously worries and intrigues physicists: What if the LHC, as well as the particle physics experiments planned at a Tevatron-less Fermilab for the next decade, finds nothing unexpected at all?

DESTINATION UNKNOWN

THERE WAS A TIME, not long ago, when physicists had many of the same hopes for the Tevatron that they now have for the LHC. Fifteen years before the LHC was turned on, physicists at Fermilab thought the Tevatron might bag the Higgs, find evidence for supersymmetry, identify the nature of dark matter, and more.

Besides netting a Nobel Prize, the discovery of the Higgs would provide the capstone to an illustrious era in physics. The Higgs boson is the last missing piece of the Standard Model, a complex theoretical edifice that describes the universe in terms of the interactions of the 17 fundamental particles. It unifies three of the four forces of nature: the strong force, which binds atomic nuclei; the weak force, which is responsible for particle decay; and the more familiar electromagnetic force. (Gravity is the only force not described by the Standard Model.) Theorists put the finishing touches on the Standard Model nearly 40 years ago, and since then every one of its predictions has been confirmed by experiment.

In 1995 the CDF and D-Zero teams made one of the most impressive confirmations with the discovery of the top quark—a massive elementary particle whose existence was first predicted in 1973. In that race, the Tevatron beat a European collider called the Super Proton Synchrotron, which is now used to feed particles into the LHC. It was the Tevatron's greatest triumph and established that the Standard Model was an incredibly accurate description of the universe, at least at the energies that physicists could probe with their best accelerators.

In 2001, after a five-year upgrade, the world's best accelerator became even better. Physicists hoped that the new, improved Tevatron would not only discover the Higgs—the last undiscovered piece of the Standard Model—but also uncover new phenomena lying beyond the Standard Model. For all the Standard Model's predictive power, physicists know that it cannot be a complete description of nature. Besides its failure to incorporate gravity, it has two other glaring shortcomings. The Standard Model provides no explanation of dark matter, which influ-

MILESTONES

Three Decades of Discovery

Most everything you need to know about a particle collider can be summed up with just two numbers. The first is its energy—higher energies let scientists conjure up more massive particles (measured in gigaelectron volts, or GeV). The second is its luminosity, or the number of collisions per second. Engineers spent the first decade of the Tevatron pushing up its energy; they've spent the past two opening a trickle of collisions into a firehose. Here are a few of the more notable events in the life of the collider.

JULY 5, 1979
The Department of Energy authorizes Fermilab to build a superconducting accelerator, later named the Tevatron.

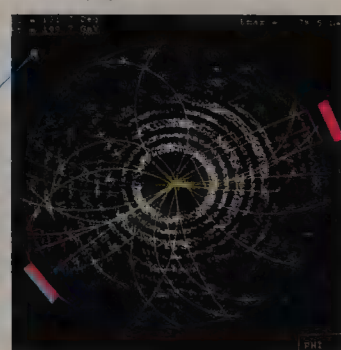
JULY 3, 1983
The Tevatron accelerates protons to a world-record energy of 512 GeV.

OCTOBER 1, 1983
Experiments begin. At first, a single beam of protons strikes a fixed target.

OCTOBER 13, 1985
The newly installed antiproton beam begins to collide with the protons. The CDF witnesses the first proton-antiproton collisions at 1,600 GeV.

AUGUST 31, 1992
The first long run of collision experiments begins at an energy of 1,800 GeV.

MARCH 3, 1995
Scientists from the CDF and D-Zero experiments announce the discovery of the top quark.



JULY 20, 2000
The DONuT experiment reports the first evidence for the direct observation of the tau neutrino.

MARCH 1, 2001
Upgrades push the energy up to 2,000 GeV, and the second collider run begins. Over the next decade its luminosity will more than quadruple.

AUGUST 4, 2008
Tevatron scientists announce that the Higgs boson does not have a high mass of 170 GeV. More searching is required.

SEPTEMBER 30, 2011
The Tevatron produces its final proton-antiproton collisions; data analysis will continue for several years.

COURTESY OF FERMILAB

ences the motions of galaxies but otherwise does not seem to interact with ordinary matter. It also fails to account for dark energy, an utterly baffling phenomenon that appears to be accelerating the expansion of the universe.

But despite the upgrade, the Tevatron failed to move beyond the theory it had so spectacularly validated. "Ten years ago we anticipated cracking this nut, but we haven't yet," says Bob Tschirhart, a theoretical physicist at Fermilab. "There's a layer of existence out there that we haven't discovered. The Standard Model has been so good at predicting so much, but it has such obvious inadequacies. It's like an idiot savant."

In some sense, the legacy of the Tevatron is that the Standard Model works really, really well. It's no small achievement, but it was never intended to be the final goal. "We were supposed to find the Higgs, for sure," says Stephen Mrenna, a computational physicist who came to Fermilab in the mid-1990s. "And if supersymmetry was there, we were supposed to find it, too."

Physicists now hope that the LHC will succeed where the Tevatron failed by leading them into new territory and providing clues that might eventually enable them to replace the Standard Model. Mrenna, like most of his colleagues, believes that the LHC will find the Higgs sooner rather than later. "I think it will happen this year or next. That's where I would place my bet," he says. "If we don't find it, my belief that we won't find anything will go up greatly."

This is the problem with exploration: perhaps nothing is out there. Some physicists speculate that an "energy desert" exists between the realms they are able to probe now and the realm where truly new physics might emerge. If that's the case, new discoveries might be decades away. The LHC might be the most powerful accelerator ever built, but it is not so powerful that physicists can be completely sure it will punch through to another level of reality.

The real tool for that job was the Superconducting Super Collider (SSC), a machine that, at 54 miles in circumference, would have dwarfed the LHC. It would have been capable of generating particle beams with nearly three times the LHC's maximum energy. But cost overruns caused Congress to cancel the project in 1993, even though construction had already started near the small town of Waxahachie, Tex. "The SSC was designed from the beginning so that it would probe an energy scale where our expectations were that something new absolutely, positively had to happen," Mrenna says. "It really was the right collider to have built. The LHC is a cheap cousin. But it's good enough for now."

Unless, of course, it is not. If the LHC fails to find the Higgs or to make some other significant discovery, Mrenna says, it would become difficult for physicists to justify the costs of a more advanced accelerator. "You can ask what finding the Higgs boson has to do with the U.S. economy or the war on terror, or whatever," he observes, "and right now we get by saying the knowledge benefits everybody. People want to know how the universe works. And we're training lots of people, and it's always a good idea to take the cleverest people around and give them a really hard problem because usually there's a derivative that comes from it. But at some point the physics becomes less and less relevant."

In other words, if the energy desert is real, we may not be able to summon the will to cross it. "I'm actually a hanger-on from the SSC," Mrenna says. "I was a postdoc in its last year. And I have been waiting for a replacement for it ever since then, surviving in a rather grim job market. We need a success. We need to find something new."

COMPETITION

The Race against the LHC

By Geoff Brumfiel

The Tevatron's operations may be ending, but the hunt for the Higgs boson, the most elusive particle in physics, is charging forward. In a matter of months, data from the Tevatron and the Large Hadron Collider at CERN near Geneva should answer what one physicist describes as the "Shakespeare question": Is it to be? Or not to be?

For nearly half a century scientists have predicted the existence of the Higgs. It is commonly said that the Higgs is the particle responsible for the mass of all the others—which is true—but from a physicist's perspective, the Higgs is important because it serves as a unifier of forces. Physicists love to simplify, and the Higgs provides an elegant way to combine electricity and magnetism with the "weak" nuclear force to create a single "electroweak" entity.

The Higgs can only do this if it exists in the mass-energy range between 100 and 1,000 billion electron volts (GeV). The LHC and the Tevatron are closing in on the most fertile ground. In July at a conference in Grenoble, France, Tevatron scientists concluded that the Higgs cannot be between 156 and 177 GeV, while the LHC knocked out a few broad swaths between 150 and 450 GeV.

Most physicists believe that if the Higgs exists, most likely it is hiding at around 115 to 140 GeV. It is a particularly tricky energy range, however, because such a light Higgs particle will often decay into common particles that are difficult to pick out from other debris inside the giant collider. A few Higgs decays may have already been seen, but telling the difference will require many more times the data produced so far.

Even after its shutdown, the Tevatron will contribute yet to be analyzed data to the hunt. But it will be up to the more powerful LHC to nail the discovery. The larger European machine's current run continues through October, and in that time it should be able to firm up any faint signals. Still, physicists will not be able to announce whether the Higgs is truly "to be" until the end of 2012, when the machine will have collected around 50 petabytes of data—the equivalent of the complete works of Shakespeare 10 billion times over.

Geoff Brumfiel is a reporter for Nature.

NEXT LIFE

THE WORLD'S FIRST particle accelerator was made in 1929 by Ernest Lawrence, a physicist at the University of California, Berkeley. He called it a proton merry-go-round. It measured five inches across, was made of bronze, sealing wax and glass, and likely cost about $25. The LHC, which fired up about 80 years later, cost $10 billion. Its construction required an interna-

tional effort, and it covers an area the size of a small town. Even if the LHC is wildly successful, there is little chance for a similar leap in scale in the foreseeable future.

"We know how to go 10 times higher in energy, but it would cost 10 times more," says Pier Oddone, director of Fermilab. "And we're already at the limit of what countries are willing to spend."

For the next decade and beyond the premier physics facility in the U.S. will live in the shadow of the LHC. Oddone says Fermilab will pursue a variety of projects that might have been delayed or canceled had the Tevatron remained in operation, but it is clear that the center of mass in the world of particle physics has shifted. "In an ideal world, we would have kept the Tevatron running without shutting down other stuff," he says. "But the money wasn't there." Experiments are now under way at Fermilab that will study the physics of neutrinos—probably the least understood of all fundamental particles—by shooting them from a source at Fermilab through 450 miles of the earth's crust toward a detector in a mine shaft in Minnesota. Fermilab scientists will also take part in the Dark Energy Survey, an astronomical investigation into the nature of dark energy.

But the overriding institutional goal is to once again host the world's most powerful particle accelerator. By 2020 Oddone hopes the lab will have completed construction of an accelerator called Project X. The near-term purpose of the mile-long machine will be to generate neutrinos and other particles for experiments at Fermilab. In the long term, the relatively small accelerator will serve as a test bed for technologies that might one day make it possible to build an affordable successor to the LHC.

"Project X is a bridge to getting back to the high-energy frontier of physics," says Steve Holmes, the project manager. "It's an opportunity to grab the leadership position and hold it. When people at lunch ask me what's the future for us here, I say that the U.S. led the world in high-energy physics for 70 years. It's the most fundamental field of physics, and as a great country we have to aspire to do that. What I can't tell them is when we'll get there."

We may not have heard the last from the Tevatron itself. Denisov, Roser and their colleagues at the old accelerator's two detectors have collected enough data to keep them busy for at least two years after the shutdown. The huge store of data could help flesh out initial discoveries made by the LHC. There is even an outside chance that some new result lies buried on a hard drive somewhere at Fermilab, just waiting to be analyzed. For a little while this past spring, it looked as if the Tevatron might have given us the first hint of physics beyond the Standard Model.

In April, Roser's CDF team announced that it had found very tentative evidence for a new particle or force of nature in data collected by the CDF. In a small but statistically significant number of cases, the physicists found a bump in the data, an excess of particles above what the Standard Model predicted. The particles appeared to be the decay products of some more massive particle, perhaps an unexpected form of the Higgs boson.

By the end of May the CDF team had analyzed the data again. "The bump is still there," Roser said at the time. Less than two weeks later, though, Roser's longtime colleague and rival Denisov said that the D-Zero team had completed an independent analysis of the CDF data. "We saw nothing," he said at a press conference.

It is not yet clear whether the bump will survive further scrutiny. The two groups are now comparing their results to see where the CDF analysis may have erred—if indeed it did err. For now, it looks like a new era in physics is on hold, as it has been for more than 30 years. It will be a shame if the bump vanishes. Discovering the Higgs would have made for quite an exit for the Tevatron. Within the next year or so we might all find out if the LHC can do any better.

Ready, aim: **The Tevatron (*central ring*) is going dark, but physics continues at Fermilab. Scientists are generating neutrinos using the smaller injector ring (*lower left*) and beaming them through the earth to an underground detector in Soudan, Minn., 450 miles away.**

COURTESY OF FERMILAB

MORE TO EXPLORE

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Three decades of discovery: Explore a visual history of the Tevatron at ScientificAmerican.com/oct2011/tevatron

Gareth Dyke is a paleontologist at the University of Southampton in England, where he studies the evolutionary history of dinosaurs and birds. He is writing a novel inspired by Baron Franz Nopcsa's life with István Főzy of the Hungarian Natural History Museum in Budapest.

PALEONTOLOGY

THE DINOSAUR BARON OF TRANSYLVANIA

A maverick aristocrat's ideas about dinosaur evolution turn out to have been decades ahead of their time *By Gareth Dyke*

THE YEAR IS 1906. A SMALL, NATTILY DRESSED MAN WALKS OVER TO THE giant *Diplodocus* skeleton in the entrance hall of the British Museum of Natural History. He gently lifts one of the dinosaur's huge toe bones out of its iron mount, flips it over and carefully slips it back into place. Later he would note in correspondence to a colleague that his effort was not appreciated. The museum officials should have known better. The visitor was Franz Nopcsa (pronounced "nop-cha"), baron of Szacsal in Transylvania. In addition to being a nobleman, he was an esteemed authority on dinosaurs and other fossil animals. The baron had noticed that the *Diplodocus* toe bone was oriented incorrectly and was simply trying to fix it. Although Nopcsa failed to garner the respect of the officials, history has been somewhat kinder to him. Among paleontologists today, he is well known for having discovered and described some of the first dinosaurs from central Europe. Yet the details of Nopcsa's personal life have often overshadowed his intellectual legacy. Adventurous, eccentric and wildly ambitious, Nopcsa was a colorful character. He served as a spy in World War I and made a bid to become king of Albania. He was also openly homosexual; his lover and secretary was a much younger Albanian man named Bajazid Elmaz Doda.

But there was much more to Nopcsa than his fossil collection and his personal and political affairs, as recent findings have underscored. He pioneered techniques for fossil analysis that are still at the forefront of paleontological research. Moreover, his theories about dinosaur evolution turn out to have been decades ahead of their time. Nopcsa insisted that his Transylvanian dinosaurs were key to understanding dinosaur evolution on a global scale. Only in the past few years, with new fossil discoveries, have scientists begun to appreciate how right he was.

ISLAND OF DWARFS

NOPCSA FIRST ENCOUNTERED FOSSILS in 1895, when his sister, Ilona, happened on some large bones on one of the family estates in Transylvania, then part of Austria-Hungary. He pounced on the remains and brought some to Vienna, where he was attending secondary school, to show to a geology professor. The professor

informed him they were from dinosaurs and offered him the assistance of one of the department technicians to collect more remains and to prepare a formal description. But although he had hardly any training in paleontology, the 18-year-old Nopcsa decided to go it alone, working day and night to learn anatomy. He was quick: within a year he wrote a paper on Ilona's bones describing a new species of ornithopod dinosaur from Transylvania, later dubbed *Telmatosaurus*.

It was the beginning of a long and productive career for Nopcsa: over the next 35 years he published more than 100 scientific papers on fossils, many of them cutting-edge. He was one of the first to investigate whether the anatomy of long-extinct animals and how they had been fossilized together could be used to understand how they interacted in life; he championed the Victorian notion that birds were a kind of dinosaur, rather than the distant reptilian relatives his colleagues believed them to be—a view that has since gained acceptance by the vast majority of modern paleontologists; he charted the geology of enormous swaths of central Europe—the list goes on and on.

Nopcsa traveled far and wide in his scientific pursuits, but his most important work derived from discoveries made in his own backyard. The baron noticed, for example, that *Telmatosaurus,* the dwarf sauropod *Magyarosaurus* (a genus name coined by German paleontologist Friedrich von Huene to replace Nopcsa's use of *Titanosaurus*) and other dinosaurs found on the Nopcsa estates were significantly smaller than other closely related species. *Magyarosaurus,* for one, was just six meters long—tiny compared with other sauropods, which routinely reached lengths of 15 to 20 meters. Because Nopcsa was an accomplished geologist, he knew that back when *Magyarosaurus* roamed Transylvania some 70 million years ago, at the end of the Cretaceous period, a warm, shallow sea called Tethys covered much of southern Europe, leaving only islands of elevated regions suitable for terrestrial creatures. He also knew that some island-dwelling mammals, such as the recently extinct Mediterranean elephants, had evolved small bodies, presumably an adaptation to the limited resources available in these environments. Putting two and two together, he proposed in 1914 that the burial ground of his dinosaurs had once been part of an island born of the flooding of Europe by the Tethys Sea. He called this putative island Hátszeg and argued that his dinosaurs had attained their pint-size proportions as a result of island dwarfing.

Although Nopcsa's contemporaries would have known about the pony-size elephants from Crete and other Mediterranean islands, no one had ever proposed that such shrinking could occur in dinosaurs. The baron's bold theory was largely ignored. But starting in the late 1970s, renewed interest in the Late Cretaceous beasts of Transylvania put Nopcsa's dwarfing scenario back on the table. Since then, it has gained considerable support, in part because discoveries of other dinosaurs have confirmed that the Hátszeg dinosaurs were significantly smaller than their counterparts elsewhere in Europe, as well as those in Asia and North America.

Ancient islands such as Hátszeg, formed by a sea that covered much of southern Europe during the Late Cretaceous, served as stepping-stones for dinosaurs on the move and allowed them to evolve to a small body size.

Recently my own work has bolstered Nopcsa's ideas. In studying a collection of Early Cretaceous bones unearthed from a Transylvanian bauxite mine in the 1970s, I discovered a number of very small birds and pterosaurs represented among the remains. Judging from preserved wing elements, I surmised that the creatures were probably capable of flying long distances. As I reported last year in a paper published in *Palaeontology,* these are exactly the kinds of flying animals one would expect to find on an isolated island. In fact, the species preserved in the bauxite mine collection are similar to the ones Nopcsa found in Hátszeg, a few hundred kilometers to the east. The bauxite mine locality was part of another earlier island in the Cretaceous archipelago formed by the Tethys.

Fittingly, evidence obtained using a technique Nopcsa himself invented has provided some of the strongest support for his island-dwarfing theory. In the 1930s Nopcsa published a revolutionary paper in which he described having exploited the microscopic structure, or histology, of bone to show that a fossil of an allegedly new type of duck-billed dinosaur from North America was actually just a juvenile member of a previously known species. He had figured out that he could estimate how old an animal was when it died based on the histology visible in thin slices of bone when viewed under high magnification, much as one can count growth rings to determine the age of a tree.

IN BRIEF

Franz Nopcsa was a turn-of-the-century Transylvanian nobleman who loved fossils.

Although best known for his personal and political exploits, he also pioneered techniques for fossil analysis and formulated theories about dinosaur evolution and dispersal around the globe.

Recent discoveries underscore that Nopcsa's scientific ideas were remarkably prescient.

SOURCE: "AN UNUSUAL DINOSAUR FROM THE LATE CRETACEOUS OF ROMANIA AND THE ISLAND RULE," BY HANS-DIETER SUES, IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA,* VOL. 107, NO. 35; AUGUST 31, 2010 (*islands*); *THE CHANGING FACE OF THE EARTH,* BY BRUNO VRIELYNCK AND PHILIPPE BOUYSSE; UNESCO PUBLISHING/COMMISSION OF THE GEOLOGICAL MAP OF THE WORLD, 2003 (*world*)

Map by Emily Cooper

One of the weak spots in Nopcsa's dwarf dinosaur theory, when he first proposed it, was that he could not exclude the possibility that his dinos were small simply because they were juveniles. He passed away before he could apply his histology technique to the problem. But recently a group of German, American and Romanian paleontologists conducted histological studies on *Magyarosaurus* and concluded that the dainty sauropod was indeed fully grown, upholding Nopcsa's interpretation of the remains as those of an island dwarf. The team published its findings last year in the *Proceedings of the National Academy of Sciences USA*.

Bone histological studies, now standard among paleontologists, have also cast light on other subjects dear to Nopcsa, including bird evolution. For example, in 2009 researchers from Germany, the U.S. and China reported in *PLoS ONE* that some early birds—the 140-million-year-old *Archaeopteryx* among them—have bone structures that show they grew up to a third as fast as living birds do, exhibiting a pattern more in keeping with "cold-blooded" reptiles than today's "warm-blooded" avians. Thus, some of the hallmark characteristics of living birds, such as their extremely fast growth rates, must have taken longer to evolve than scientists previously thought.

DINOSAURS ON THE MOVE

THE SIGNIFICANCE of Nopcsa's Transylvanian dinosaurs extends well beyond their implications for island-dwarfing theories, as the baron himself knew. Because most of Europe lay under the Tethys Sea during the Late Cretaceous, the Transylvanian specimens offer a rare glimpse of European dinosaurs from this period. Intriguingly, many of the forms found there—including the Hátszeg ornithopod *Telmatosaurus*—have counterparts only in Asia or North America—not in the Southern Hemisphere. This distribution pattern suggests that Transylvania was an important bridge between Europe and the Late Cretaceous landmass comprising Asia and North America. Dinosaurs in Europe could cross the Tethys into Asiamerica, and vice versa, by hopping along Hátszeg and the other islands that formed an archipelago stretching from the European Alps to Southwest Asia.

New geologic data published last year in *Palaeogeography, Palaeoclimatology, Palaeoecology* has shown that because Hátszeg was close to both the European continental margin and to the open ocean, it probably provided a convenient stepping-stone for animals moving from east to west. Thus, the dinosaurs of Transylvania in general, and of Hátszeg in particular, will most likely prove critical to understanding the global distribution of dinosaurs just before the zenith of their diversity 65 million years ago—a heyday cut short by a cataclysmic asteroid impact that extinguished their kind.

Forged at a time when the sciences of paleontology and geology were still young and evolution was still hotly debated, Nopcsa's theories were astonishingly prescient. No doubt they benefited from his standing as a member of the aristocracy. Because of his wealth and influence at the court of the emperor of Austria-Hungary, Nopcsa had huge advantages over the average scholar of his day. He could travel freely throughout the empire on fossil-hunting expeditions and make regular pilgrimages to the great museums of Europe. He seemed to relish these escapes from court life, readily shedding his Viennese nobleman's finery for rough, native shepherd dress when he set out for the Balkans. Conversant in several Albanian dialects, Nopcsa would disappear into the hills of Albania, often for months or years at a time, with only his secretary and lover, Doda, for company. Although he produced an immense wealth of geologic, meteorological and ethnographic data over more than a decade of Albanian travel, much of it published in the leading scientific journals of the age, it is unlikely that Nopcsa took leave from the court purely for academic reasons: in 1923 he named a new 70-million-year-old fossil turtle he had collected in Transylvania *Kallokibotion bajazidi*, the genus name meaning "beautiful and round," in honor of Doda.

Unfortunately for Nopcsa, world events conspired to strip away his privilege. After the defeat in 1918 of Germany and its allies, including Austria-Hungary, Transylvania was ceded to Romania. He lost his estates and income as a result and began to worry about how he would continue to support his itinerant scientific lifestyle. To make ends meet, he accepted a position as head of the Hungarian Geological Institute and moved to Budapest. The constraints of institutional life did not suit the freewheeling Nopcsa, however, and after just a few years he left his post to resume traveling with Doda by motorcycle in the Alps and in Italy, searching for fossils and mapping geologic features. To raise money to live on, he sold most of his fossil collection, including his treasured Transylvanian dinosaurs, to the British Museum of Natural History (now known as the Natural History Museum in London), a place he once had visited regularly as an honored scientific guest.

In the months before he died, Nopcsa received an invitation to address the Geological Society in Antwerp, Belgium. Although he was running a high fever, he made the trip. But he fell seriously ill the night before he was due to talk. Nevertheless, with no preparation, he delivered a lecture on the geology of Albania in French to a packed hall. "Whenever I talk," he later wrote to a friend back in Budapest, "the room is filled mostly with ladies who hope for fewer scientific explanations than adventure stories." Surely the swashbuckling dinosaur baron was happy to indulge them.

Alas, Nopcsa's life ended in tragedy. On April 25, 1933, the great fossil hunter, by now destitute and depressed, served Doda a drug-laced cup of tea and then fatally shot his sedated lover in the head before turning the gun on himself. The heartbreaking suicide note he left for police said, "The reason for my suicide is my nervous system, which is at its end. The fact that I killed my long-term friend and secretary, Mr. Bajazid Elmaz Doda, in his sleep, without him having an inkling as to what was going on, was because I did not want to leave him behind sick, in misery and in poverty because he could have suffered too much." The baron may be long gone, but his scientific legacy continues to grow. SA

MORE TO EXPLORE

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SCIENTIFIC AMERICAN ONLINE
See a timeline of Nopcsa's discoveries and later work that validated his claims at ScientificAmerican.com/oct2011/dinobaron

BIOLOGY

Actuary of the Cell

Building on her Nobel Prize–winning research on cell function, Elizabeth H. Blackburn is trying to find a simple measure of a person's health risks

Interview by Thea Singer

A MOLECULAR TIMEPIECE THAT RESIDES INSIDE EACH CELL STILL MAKES HEADLINES, decades after Elizabeth H. Blackburn conducted pioneering studies into how it works. The most recent experiments by Blackburn and other researchers have demonstrated that these cellular clocks, known as telomeres, may act as barometers of whether a person will remain healthy or not.

IN BRIEF

WHO
Elizabeth H. Blackburn

LINE OF WORK
A cell and molecular biologist, Blackburn researches the structure and functioning of the DNA that caps the ends of chromosomes.

WHERE
University of California, San Francisco

BIG PICTURE
Blackburn has extended her Nobel Prize–winning work on telomeres to develop measures that aim to assess overall risks for heart disease, cancer and other chronic illnesses.

Telomeres, stretches of DNA at the ends of chromosomes, protect chromosomes from fraying and sticking to one another. But every time a cell divides—as immune and skin cells do—the telomeres get a little shorter. This shortening has made telomeres a marker of cellular aging. In some cells, an enzyme called telomerase replenishes lost segments. In other cells, though, shortening goes on unimpeded. When the telomere erodes past a certain point, the cell stops dividing and either enters an arrested state of senescence or dies. Blackburn and her one-time graduate student Carol W. Greider, now at Johns Hopkins University, along with Jack W. Szostak of Harvard Medical School, won the 2009 Nobel Prize in Physiology or Medicine for elucidating many of these processes.

Blackburn, who is based at the University of California, San Francisco, has never stopped to catch her breath. In 2004 she and health psychologist Elissa S. Epel published a paper linking psychological stress with telomere shortening in white blood cells. It lit a fire under telomere research. Today numerous studies show connections between shorter telomeres and various diseases. Conversely, longer telomeres have been tied to behaviors such as exercise and stress reduction. These studies have pointed to the direct possibility of using telomere length, measured through a simple blood test, to

Photograph by Cody Pickens

provide a snapshot of overall health and a glimpse into the aging process.

Last year Blackburn co-founded a company, Telome Health in Menlo Park, Calif., to offer that blood test both to research centers as well as to individuals through medical providers. Another group has launched a telomere-testing company, Life Length, in Madrid. News of the imminent release of these tests ignited a controversy about their usefulness. Science writer Thea Singer recently spoke to Blackburn about her work. Excerpts follow.

Scientific American: We've heard a lot about how cells "age" as telomeres shorten. But how does this shortening relate to the aging of the whole body?

BLACKBURN: Many studies show that telomere shortness anticipates risk for conditions such as cardiovascular disease, diabetes, Alzheimer's and certain cancers—and even for mortality. In part of my U.C.S.F colleague Mary Whooley's Heart and Soul Study that followed 780 people in their 60s and older for four years, telomere shortness proved a risk for mortality. University of Utah geneticist Richard Cawthon followed 143 people for 15 to 20 years and found that the mortality rate for those with shorter telomeres was nearly double that of people with longer telomeres.

Perhaps, then, we should change the way we talk about telomere shortening and replace words like "aging" and "cellular aging" with phrases like "risk for diseases of aging."

Yep, I think so. I don't like the aging idea, because I think that it is not quite so helpful.

What evidence is there that life events such as chronic stress and childhood trauma relate to shorter telomeres?

Let's look at childhood trauma. The studies find that the number of childhood traumas relates, quantitatively, to the degree of telomere shortness in the adult: the more traumas, the shorter the telomeres. Our study showed a striking correlation between the number of years of chronic stress experienced by the caregiver mothers of a chronically ill child and the degree of telomere shortness.

Long-term studies also indicate that we may be able to slow telomere shortening—or even lengthen our telomeres—through behaviors such as diet and exercise. Tell me about this.

Looking at people with stable coronary artery disease over five years, we found that those with higher levels of marine omega-3 fatty acid in the blood had less telomere shortening overall and that those whose telomeres actually lengthened over the five years were much more likely to have started with higher omega-3 levels. We have data on what has happened to those people, but they have not been published yet.

Should I up my dosage of omega-3?

These subjects are in their 60s by now and have mild coronary disease, which was steady at the onset of the study. So these results relate to those people. It may not be true for people who are 80 or 90 or who are 15 to 20.

You've said that the "old medical model" focuses on running tests to decide which treatments can best eradicate an infectious agent. But today doctors very frequently grapple with chronic diseases that arise over time from a complex of causes. How does telomere research contribute to this new model?

Telomere research doesn't usually look at a specific diagnosis per se. For most people, what we see are statistical relations with a set of progressive diseases that often go together and are more prevalent with aging. We think they may have some similar underlying biology. People are very interested in the idea that chronic inflammation—which may be read out by telomere shortness in white blood cells or perhaps even caused in part by telomere shortness—might underlie some of these things that we separately call, say, diabetes and cardiovascular disease and treat separately. Telomere length is one number that captures a multitude of physiological influences.

Do you think clinicians are catching up with this perspective?

I think clinicians want to find out what is actionable. I think the idea of using telomere length as a monitoring device—that might be actionable.

Your paper on "cancer interception"—using drugs and other active means to stop cancer before it becomes established—dovetails with this concept.

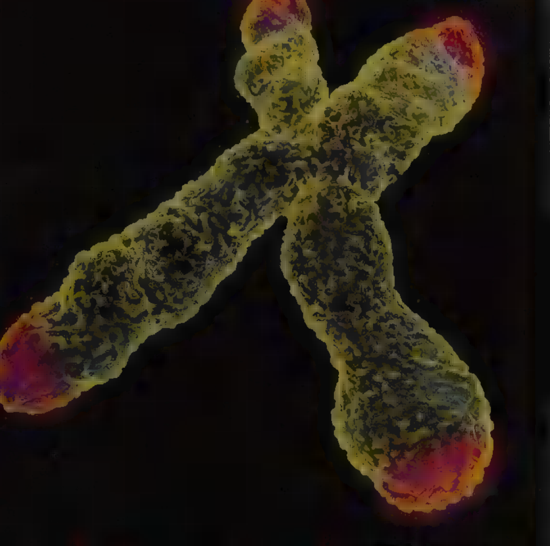
That's right. The point is to intercept early—before you get to the stage of full-blown disease, which has huge human and economic costs. Cancer research has led us to understand earlier and earlier stages of cancers and how cancers progress. So now we know that a particular drug might actually work at a very early stage in a given cancer. That idea, carried to its extreme, would be: perhaps we can think of what the risk factors are for people to even develop certain cancers and can then treat them before disease strikes. Researchers are looking at high-risk groups for some colon cancers, and there are certain ways of intercepting them, for example.

Where do telomeres fit into the interception picture?

In mice, it's clear that telomere shortness is a dramatic cancer risk. We still have to learn how that plays out in humans. But it's been seen in cohorts of people; if you look at, say, risks for groups of cancers or some individual cancers, telomere shortness predicts later risk. This could be because the immune system—which is what you're querying when you look at telomeres in white blood cells—is getting compromised. Or it could be that there's a chronic inflammatory state, which is promoting the cancer. Or the cancer cells themselves have genomic instability because their telomeres are too short, and that's promoting cancer.

Is there a genetic component to telomere length and cancer risk?

Jian Gu of the University of Texas M. D. Anderson Cancer Center led an interesting study implying that the answer is sometimes yes. He and his colleagues



Harbingers of mortality: Telomeres at chromosome tips glow brightly here.

took an unbiased look to see if telomere shortness and cancer risk went together genetically. The paper they published concentrated on bladder cancer. They asked: What variance in the genome is associated with risk of cancer? And they found a genetic variant that went with both telomere shortness and cancer risk. Then they looked for the gene itself and found it was one associated with immune cell function.

Recent headlines say that telomere tests for individuals will tell you how long you'll live. Please explain, based on the science, what it is that telomere tests will tell us.

The business that somehow the test will predict how long you'll live—that's what I call silly. The test is not going to diagnose a disease. And it won't tell you if you're going to live to be 100. But over time, if you look at it statistically, it tells you probabilities—that, say, you have a likelihood that you might or might not be more prone to get some of the common diseases of aging. A company in addition to ours that formed to measure telomere length gave itself the name "Life Length," which I think started meaning certain things to people. That was probably an unfortunate name.

What's the most beneficial way to use the test's measurements?

We don't know yet whether there is an optimum way. We do know you can see telomere-length changes in six months or even four months but not in a week. Based on scientific principles, the more measurements you can plot on a curve, the better you can see trends. So the six-month approach seems reasonable.

The test sounds similar to cholesterol tests: it gives you a percentile—where you fall relative to a norm for people of similar age, gender, lifestyle behaviors, and so on.

That's right, although cholesterol more specifically relates to cardiovascular disease. The telomere test is more general. You could think of it as weight: weight can be an indicator of many aspects of health. Clearly, if it's way too high, that's not good. Likewise, if telomeres are really, really short, that's not good. But then there's a whole range. And doctors use weight, right? It's a useful thing. And they look at it over time. I think telomere length is similar; it's a number that integrates many different things. And clinically, you wouldn't use it alone.

Critics of telomere testing have said that cholesterol tests are useful because enough data exist to permit scientists to establish norms for things like "high" and "low" cholesterol but that there are not enough data yet to establish norms for telomere length.

I don't think that's true. Scientists are sophisticated these days—we don't have to lump everyone together. We can put people into groups. There are now hundreds and thousands of telomere lengths in various cohorts, and I think we have a decent idea of what sort of things to expect. Of course, more is always better. But you have to start somewhere. There was a very strong demand for getting telomere measures done both in research settings and among individuals. The idea was that we could start getting these measures out there without overstating the precision of what you can deduce from them.

Why did you decide to start a company rather than doing the measurements in your lab at U.C.S.F.?

It was important to have a responsible, reliable technology for providing such measurements. We were overwhelmed in our ability to handle all the requests at U.C.S.F., so we transferred the technology to the company.

How do you respond to concerns that life and medical insurance companies might use telomere-test results to determine eligibility for coverage?

We can't hide information. But we can certainly try to make sure that any clinical information we provide is accurate and is taken in the proper context and not misused scientifically for exclusionary reasons. Besides, given that telomere-test measurements provide only probabilities, they'd be a poor source for making such decisions. But it's something that one has to keep thinking about. Our aim is to provide the tests as a way to help people take greater charge of their own health.

Critics compare telomere tests with the sometimes hyped direct-to-consumer genetic tests that offer to find your genetic variations and tell you your susceptibility to certain diseases. How are these telomere tests different?

The telomere tests are not direct-to-consumer. We should be very clear. We plan to start offering them in October through health professionals. Multiple cohorts and multiple studies have established clear statistical links with telomere shortness and risks for diseases. Telomere science has been emerging at a rapid pace recently, and it's sometimes hard for scientists not involved in such studies to keep up.

Are you getting your own telomeres measured?

Yes, when the company starts offering individual tests. I look forward to it. ■

Thea Singer is a Boston-based science writer.

MORE TO EXPLORE

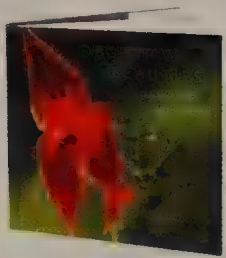
Stress Less. Thea Singer. Hudson Street Press, 2010. An investigation of stress, telomeres and aging.

Decoding Immortality. A Smithsonian Channel documentary about Blackburn's work: www.smithsonianchannel.com/site/sn/show.do?show=137613

Elizabeth Blackburn's 2009 Nobel lecture: http://nobelprize.org/nobel_prizes/medicine/laureates/2009/blackburn-lecture.html

SCIENTIFIC AMERICAN ONLINE
Read more of the interview with Blackburn at ScientificAmerican.com/oct2011/blackburn

Recommended by Kate Wong



Deceptive Beauties: The World of Wild Orchids

by Christian Ziegler.
University of Chicago Press,
2011 ($45)

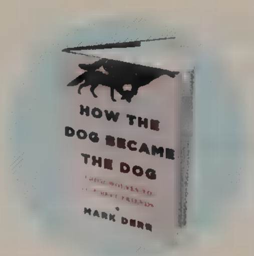
Orchids are experts in the art of seduction. They have acquired all manner of adaptations aimed at tricking insects into helping them propagate. Photographer Christian Ziegler captures these sex symbols of the plant world in 150 portraits taken on five continents in environments ranging from tropical cloud forest to semidesert.

Prosthechea chacaoensis

World in the Balance: The Historic Quest for an Absolute System of Measurement

by Robert P. Crease. W. W. Norton, 2011 ($26.95)

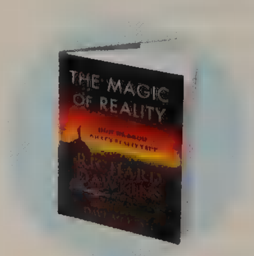
Philosopher Robert B. Crease of Stony Brook University charts the evolution of measurement from the regional systems developed to serve local needs to the universal system adopted by nearly every country on earth—a shift "as startling as if the entire world came to speak one language."



How the Dog Became the Dog: From Wolves to Our Best Friends

by Mark Derr. Overlook, 2011 ($26.95)

Thousands of years ago, probably somewhere in the ancient Near East, Fido got his start. Mark Derr, author of two previous books on dogs, traces the origin and evolution of man's best friend from its wild wolf ancestors and explores how the bond between humans and dogs was forged.



The Magic of Reality: How We Know What's Really True

by Richard Dawkins. Free Press, 2011 ($29.99)

Evolutionary biologist Richard Dawkins teams up with illustrator Dave McKean to create a graphic science book addressing questions ranging from "Who was the first person?" to "What is a rainbow?" For each phenomenon, Dawkins details both the mythologies people initially developed to make sense of it and the actual explanation, as revealed by science.

ALSO NOTABLE

Plastic Ocean: How a Sea Captain's Chance Discovery Launched a Determined Quest to Save the Oceans, by Charles Moore, with Cassandra Phillips. Avery, 2011 ($26)

But Will the Planet Notice? How Smart Economics Can Save the World, by Gernot Wagner. Hill and Wang, 2011 ($27)

The Sibling Effect: What the Bonds among Brothers and Sisters Reveal about Us, by Jeffrey Kluger. Riverhead, 2011 ($26.95)

America the Vulnerable: Inside the New Threat Matrix of Digital Espionage, Crime, and Warfare, by Joel Brenner. Penguin Press, 2011 ($27.95)

Galileo's Muse: Renaissance Mathematics and the Arts, by Mark A. Peterson. Harvard University Press, 2011 ($28.95)

The Great Sea: A Human History of the Mediterranean, by David Abulafia. Oxford University Press, 2011 ($34.95)

The End of the Beginning: Cosmology, Time and Culture at the Twilight of the Big Bang, by Adam Frank. Free Press, 2011 ($26)

The Fossil Chronicles: How Two Controversial Discoveries Changed Our View of Human Evolution, by Dean Falk. University of California Press, 2011 ($34.95)

The Viral Storm: The Dawn of a New Pandemic Age, by Nathan Wolfe. Times Books, 2011 ($26)

Deadly Monopolies: The Shocking Corporate Takeover of Life Itself—And the Consequences for Your Health and Our Medical Future, by Harriet A. Washington. Doubleday, 2011 ($28.95)

Lifeblood: How to Change the World One Dead Mosquito at a Time, by Alex Perry. Public Affairs, 2011 ($25.99)

CHRISTIAN ZIEGLER *Minden Pictures*

COMMENT AT ScientificAmerican.com/oct2011

Think Clearly.

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Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com). His new book is *The Believing Brain*. Follow him on Twitter @michaelshermer

The Decline of Violence

Be skeptical of claims that we live in an ever more dangerous world

On July 22, 2011, a 32-year-old Norwegian named Anders Behring Breivik opened fire on participants in a Labour Party youth camp on the island of Utoya after exploding a bomb in Oslo, resulting in 77 dead, the worst tragedy in Norway since World War II.

English philosopher Thomas Hobbes famously argued in his 1651 book, *Leviathan*, that such acts of violence would be commonplace without a strong state to enforce the rule of law. But aren't they? What about 9/11 and 7/7, Auschwitz and Rwanda, Columbine and Fort Hood? What about all the murders, rapes and child molestation cases we hear about so often? Can anyone seriously argue that violence is in decline? They can, and they do—and they have data, compellingly compiled in a massive 832-page tome by Harvard University social scientist Steven Pinker entitled *The Better Angels of Our Nature: Why Violence Has Declined* (Viking, 2011). The problem with anecdotes about single events is that they obscure long-term trends. Breivik and his ilk make front-page news for the very reason that they are now unusual. It was not always so.

Take homicide. Using old court and county records in England, scholars calculate that rates have plummeted by a factor of 10, 50 and, in some cases, 100—for example, from 110 homicides per 100,000 people per year in 14th-century Oxford to fewer than one homicide per 100,000 in mid-20th-century London. Similar patterns have been documented in Italy, Germany, Switzerland, the Netherlands and Scandinavia. The longer-term trend is even more dramatic, Pinker told me in an interview: "Violent deaths of all kinds have declined, from around 500 per 100,000 people per year in prestate societies to around 50 in the Middle Ages, to around six to eight today worldwide, and fewer than one in most of Europe." What about gun-toting Americans and our inordinate rate of homicides (currently around five per 100,000 per year) compared with other Western democracies? In 2005, Pinker computes, just eight tenths of 1 percent of all Americans died of domestic homicides and in two foreign wars combined.

As for wars, prehistoric peoples were far more murderous than states in percentages of the population killed in combat, Pinker told me: "On average, nonstate societies kill around 15 percent of their people in wars, whereas today's states kill a few hundredths of a percent." Pinker calculates that even in the murderous 20th century, about 40 million people died in war out of the approximately six billion people who lived, or 0.7 percent. Even if we include war-related deaths of citizens from disease, famine and genocide, that brings the death toll up to 180 million deaths, or about 3 percent.

Why has violence declined? Hobbes was only partially right in advocating top-down state controls to keep the worse demons of our nature in check. A bottom-up civilizing process has also been under way for centuries, Pinker explained: "Beginning in the 11th or 12th [century] and maturing in the 17th and 18th, Europeans increasingly inhibited their impulses, anticipated the long-term consequences of their actions, and took other people's thoughts and feelings into consideration. A culture of honor—the readiness to take revenge—gave way to a culture of dignity—the readiness to control one's emotions. These ideals originated in explicit instructions that cultural arbiters gave to aristocrats and noblemen, allowing them to differentiate themselves from the villains and boors. But they were then absorbed into the socialization of younger and younger children until they became second nature."

That second nature is expressed in the unreported "10,000 acts of kindness," as the late Stephen Jay Gould memorably styled the number of typically benevolent interactions among people for every hostile act. This is the glue that binds us all in, as Abraham Lincoln so eloquently expressed it, "every living heart and hearthstone all over this broad land" through "the mystic chords of memory" that have been touched again by these better angels of our nature.

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/oct2011

Illustration by Patrick Leger

Steve Mirsky has been writing the Anti Gravity column since atmospheric carbon dioxide levels were about 358 parts per million. He also hosts the *Scientific American* podcast Science Talk.

Surface Tension

Sit down, you're rocking the stadium

It's a beautiful afternoon at the ballpark, at which you have plunked down good money to be a spectator. Then it starts heading your way. From off in the distance, other members of the crowd inexplicably sacrifice their individuality and join together to get up sequentially and then briefly raise their arms to the heavens before returning to their seats. The move rolls across sections of the stands. It draws closer and closer. And then you're engulfed. Whether you took part or just sat there waiting for it to pass, you've been subsumed. You have drowned in the Wave.

But now—for the second time in one summer!—a reasonable idea has emerged from Texas. The public address announcer of the defending (as I write this in August, anyway) American League champion Texas Rangers is trying to get fans to stop the Wave. The team, though not officially endorsing a Wave ban, has taken to displaying a warning on the scoreboard that states, emphatically and uppercasedly (printed verbatim):

SURGEONS HAVE DETERMINED THAT DOING THE WAVE WILL, YES, WILL CAUSE TEARS TO THE SUPRAPINATUS MUSCLE AND THE INFRASPINATUS MUSCLE FROM THE THROWING OF INDIVIDUAL'S ARMS RAPIDLY INTO THE AIR. IN ADDITION, ANY CHILDREN DOING THE WAVE WILL BE SOLD TO THE CIRCUS. DO NOT DO THE WAVE IN THE BALLPARK, DOING THE WAVE IS SAFE AT PRO FOOTBALL GAMES AND MILEY CYRUS CONCERTS.

(The other good idea to come out of the Lone Star State recently was the decision in July by the Texas Board of Education to reject antievolution supplements to high school biology textbooks. The National Center for Science Education [NCSE] reported that the supplements called "intelligent design" the scientific community's new "default position," which is true if by "default position" one means doubled over from *Pagliacci*-like paroxysms of miserable laughter. The NCSE's Joshua Rosenau also said that the supplements "are not only laced with creationist arguments, they are also remarkably shoddy, teeming with misspellings, typographical errors, and mistaken claims of fact." The use of such materials in a biology class would have been an insult to pedagogy and as antithetical to reason as would be, say, a governor who has advocated for secession deciding to then run for president.)

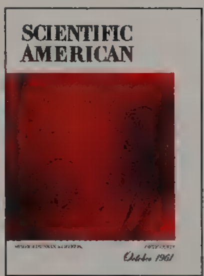
Now, I'm not against the kinds of dynamics that lead to a Wave. Some scientists have likened the Wave to the rapid and intricate movements of flocks of birds or schools of fish—the group acts as a coordinated unit without the benefit of any individual leader. Or, looked at another way, each individual becomes a leader, because its behavior informs its neighbor of the next move immediately after it gets the news from its traveling companion on the other side. Slow-motion videos conclusively show that a turn moving through a wheeling bird flock or fish school looks very much like a wave passing through a fluid, when they are not showing that an umpire has blown yet another close call.

Speaking of umpires, here's a realization I had: they're unnecessary. The obvious calls, for example, when a base runner is out by a mile, don't require an umpire. And for the incredibly close calls, the so-called bang-bang plays, the standard line is: "It could have gone either way." The hope here is that technological officiating will soon replace umpires. And any purists who argue that "human error is part of the game" can be comforted by the postgame sight of dozens of fans wandering around the parking lot trying to remember where they left their cars.

Back to the billowing, fluttering, undulating and annoying Wave. As I mentioned at the outset, when I go to a game, I pay to be a spectator. If I'm actually providing entertainment to my fellow fans, well, I want a piece of the gate. Seriously, the world's most skilled practitioners of their craft are at work on the field, and we mere mortals should pay attention. Texas is correct: keep the Wave in schools of fish and keep creationism out of schools of humans. ■

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/oct2011

Illustration by Matt Collins



October 1961

Is Bad Air Bad?

"Is air pollution in fact a menace to public health? The first place to look for damage by unclean air would be the body surfaces exposed to air: the skin, which is hardy and mainly covered by clothing, and the respiratory passages, which are not covered at all. There is evidence that a commonplace disorder of the bronchial tubes and lungs—chronic bronchitis and emphysema—is showing an alarming increase in some places. At the same time, it cannot be said that any particular atmospheric pollutant is the cause of bronchitis-emphysema or other bronchopulmonary disease, in the legal or scientific sense of the term. If something is happening to the public health from the widespread pollution of the air, it must be happening to a large number of people. Yet it must be something that goes on undramatically in its individual manifestations; otherwise it would attract public notice as an 'epidemic.'"

October 1911

Hail Costs

"In the absence of any practical method of actually averting the destructive effects of hail, the agricultural population must look to insurance to mitigate the loss to the individual sufferer. At the present time, however, hail insurance, although practiced for over a century, is founded upon a far from secure basis of information. Statistics of the distribution of hailstorms in space and time, and of the damage inflicted thereby, are systematically collected from year to year in but few countries. The first steps toward improving the organization of hail insurance and extending its benefits to all countries have been taken during the past year by the International Institute of Agriculture, Rome."

Clean Milk

"We read in a Daily Consular Report a note from Consul Mahin, of Amsterdam, in which a local periodical refers to the effect of ultra-violet beams on bacteria and to the fact that such beams are abundantly developed by mercury incandescent lamps, and relates that through this medium milk may now be sterilized in a few minutes. An apparatus has been constructed whereby the milk flows in a thin stream along an electric light. It is said the water was purified in a few minutes, without appreciably increasing its temperature."

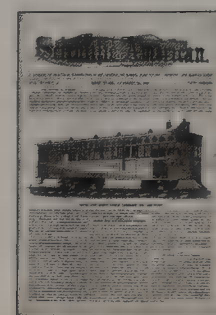
War from the Air

"The rapid development of the aeroplane for military and naval purposes [*see illustration*] behooves us to consider it most seriously in the problems of seacoast and canal fortification. We like to boast of our splendid isolation, of the steel-throated monsters that guard the entrances to our harbors. Suppose, for instance, that ten years hence, every battleship is equipped with flying machines; also that an enemy's fleet appears fifty miles off New York. Would it be necessary to pass our forts in order to destroy the metropolis? Hardly; a fleet of aeroplanes would be dispatched; within an hour they would be over the city, obeying wireless orders from their commander, and soon it would be a mass of flames. Fantastic? Possibly so."

Full text of this article is at www.ScientificAmerican.com/oct2011/aeroplane

The airplane expands its role as a weapon of war over land and sea, 1911

SCIENTIFIC AMERICAN, VOL. CV, NO. 16; OCTOBER 14, 1911



October 1861

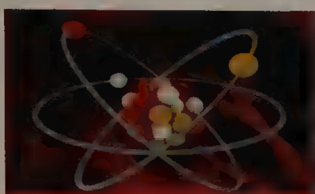
Teatime

"In consequence of the scarcity of tea in the South, the Southerners are said to be reviving the use of the Yopon or Yaupon (*Ilex cassine*), of which the North Carolina Indians made their 'black drink,' and which has been more or less used ever since in that region, though mainly by the poorer classes. The plant grows on the coast from Virginia southward, especially on the low islands which enclose Pamlico Sound. The leaves and twigs are gathered by the inhabitants and bartered for corn, bushel for bushel. It is a suggestive fact that it contains the same principle which is found in both tea and coffee and is called *theine* or *caffeine*."

Arctic Expedition

"Amid our national troubles the public seems to have forgotten the expedition of Dr. Isaac Israel Hayes and his companions to the Arctic regions, in search of more definite information regarding the open polar sea reported by Dr. Elisha Kent Kane. Since the fall of 1860, when the explorers were at Upernavic, nothing has been heard of them. In the dismal regions of perpetual snow these heroic Americans are struggling to extend geographic science amid the icebergs of the north, altogether unconscious of the more painful struggle between man and man now taking place in their native land."

The day after this went to press, news arrived by telegraph from Halifax that Dr. Hayes had arrived there safely, unsuccessful in his mission.



PARTICLE PHYSICS

Speaker: Frank Linde, Ph.D.

Quantum Questions

Welcome to the world of the infinitely small and the weird phenomena that come with it, like slow-running clocks and anti-particles. Dr Linde leads us through the discoveries, concepts, and studies in the puzzling world of quantum mechanics in a session certain to spark your curiosity about the paradoxes and possibilities quantum physics poses.

Past and Present at CERN

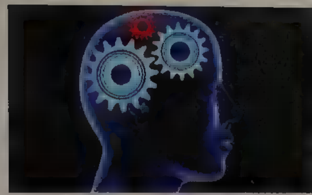
To orient us to the Large Hadron Collider (LHC)'s significance, Dr. Linde recaps the highlights of CERN's "low energy" LEP accelerator which studied the Standard Model of particle physics. Learn how physicists think the LHC experiment will address current challenges in particle physics: the origin of particle masses; the mystery of dark matter and the apparent absence of antimatter in our everyday life.

Particle Physics Matters

What has particle physics done for you today? Dr. Linde discusses the societal benefits of his research. Learn how the particle physics field leads to the development of novel technologies and applications in medicine, information technology, energy, finance and commerce, and more. Find out how basic particle research, whose significance might not be obvious, touches on all our lives.

Astroparticle Physics

Parked at the intersection of particle physics, astronomy, and cosmology, astroparticle physics is evolving rapidly. Dr. Linde guides you through the strange terrain of astroparticle physics research rooted at CERN. Hear how deep-sea neutrino telescopes search for ripples in the space-time fabric itself and how huge cosmic-ray observatories are seeking answers to the big questions.



COGNITIVE NEUROSCIENCE

Speakers: Stephen Macknik, Ph.D. & Susana Martinez-Conde, Ph.D.

How the Brain Constructs the World We See

All our understandings of our life experiences are derived from brain processes, and are not necessarily the result of an event in the real world. Neuroscientists are researching the cerebral processes underlying perception to understand our experience of the universe. Discover how our brain constructs, not reconstructs, the world we see.

Windows on the Mind

What's the connection behind eye movements and subliminal thought? Join Drs. Macknik and Martinez-Conde in a look at the latest neurobiology behind microsaccades: involuntary eye movements that relate to perception and cognition. Learn how microsaccades suggest your bias toward certain objects, their relationship to visual illusions, and the pressing questions spurring visual neurophysiologists onward.

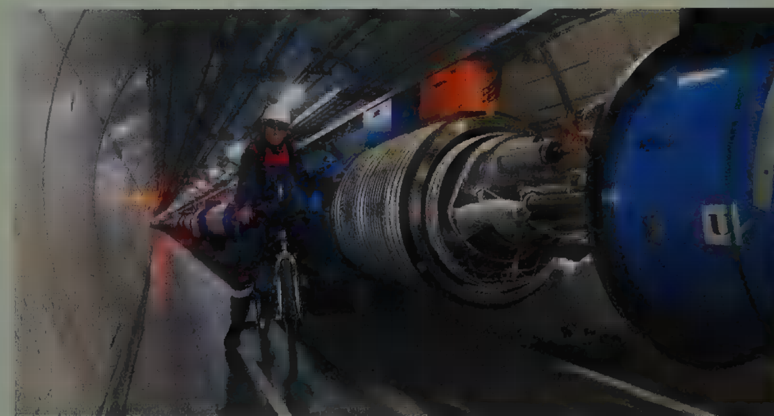
Champions of Illusion

The study of visual illusions is critical to understanding the basic mechanisms of sensory perception, and helps with cures for visual and neurological diseases. Connoisseurs of illusion, Drs. Macknik and Martinez-Conde produce the annual "Best Illusion of the Year Contest" . Study the most exciting novel illusions with them, and learn what makes these illusions work.

Sleights of Mind

Magic fools us because humans have hardwired processes of attention and awareness that are hackable. A good magician uses your mind's own intrinsic properties against you. Magicians' insights, gained over centuries of informal experimentation, have led to new discoveries in the cognitive sciences, and also reveal how our brains work in everyday situations. Get a front-row seat as the key connections between magic and the mind are unveiled!

SCIENTIFIC AMERICAN Travel HIGHLIGHTS



PRIVATE, INSIDER'S TOUR OF CERN

April 20, 2012 — From the tiniest constituents of matter to the immensity of the cosmos, discover the wonders of science and technology at CERN. Join Bright Horizons for a private post-cruise, custom, full-day tour of this iconic facility.

Whether you lean toward concept or application there's much to pique your curiousity. Discover the excitement of fundamental research and get a behind-the-scenes, insider's look of the world's largest particle physics laboratory.

Our full day will be led by a CERN physicist. We'll have an orientation; visit an accelerator and experiment; get a sense of the mechanics of the large hadron collider (LHC); make a refueling stop for lunch; and have time to peruse exhibits and media on the history of CERN and the nature of its work.

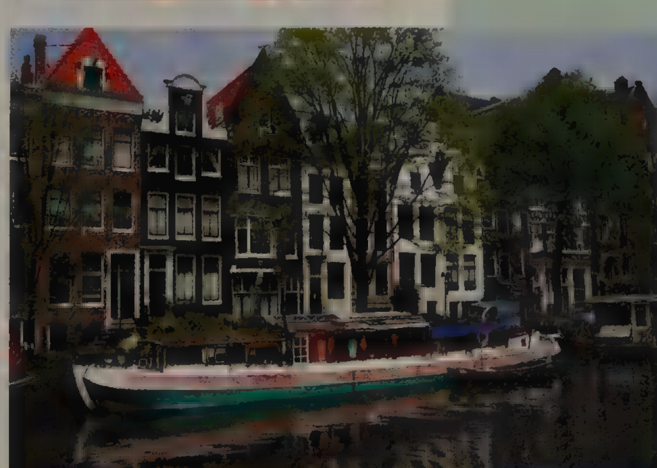
This tour includes: • transfer from Basel (end of cruise) to our Geneva hotel (April 19) • hotel (3 nights) — the nights of April 19, April 20, and April 21 • full breakfasts (3) — April 20, 21, and 22 • transfer from hotel to CERN and back to the hotel on April 20 • lunch at CERN • cocktail party the evening after our visit to CERN (April 20) • free day in Geneva; transfers to/from downtown provided (April 21) • transfer to airport for return home (April 22)

The price is $799 per person (based on double occupancy). This trip is limited to 50 people. NOTE: CERN charges no entrance fee to visitors

INSIDER'S TOUR OF THE MPIA

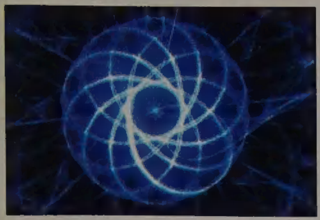
Private tours of Max Planck Institute for Astronomy (MPIA) and the newly opened Center for Astronomy Education and Outreach on April 16, 2012 (mid-cruise) ($275 pp, includes elegant lunch)

We'll board a bus to Heidelberg right after breakfast. Our tour will include a visit to the Max Planck Institute for Astronomy, a presentation at the Center for Astronomy Education and Outreach including a planetarium show about the latest astronomical research done in Heidelberg, followed by a brief visit to the historical instruments of the Landessternwarte founded by Max Wolf in 1898. We'll conclude our excursion with a memorable lunch in downtown Heidelberg.



A FULL DAY IN AMSTERDAM

What makes Amsterdam a perennial favorite? InSight Cruises invites you to find out on a private, full-day tour of "the Venice of the North". Discover the unique charms of Amsterdam as you get oriented with a coach tour of cultural touchstones. Then anchor your vacation album with images from your cruise through the city's tree-lined UNESCO World Heritage canals, getting a superb view of 17th century gabled homes, old bridges, and bicycles and more bicycles. We focus on the finest, savoring an Old Dutch welcome and contemporary cuisine at one of Amsterdam's best restaurants, and then paint ourselves into the scene at the Rijksmuseum with a visit to "The Masterpieces" exhibit. Start your Bright Horizons memories and fun and join us! $275 pp.



JAMES GILLIES, PH.D.

Particle Physics: Using Small Particles to Answer The Big Questions

Particle physics is the study of the smallest indivisible pieces of matter — and the forces that act between them. Join Dr. Gillies and catch up on the state of the art and challenges ahead as physicists continue a journey that started with Newton's description of gravity. We'll look at the masses of fundamental particles, dark matter, antimatter, and the nature of matter at the beginning time.

The Large Hadron Collider: the World's Most Complex Machine

The LHC is a machine of superlatives — a triumph of human ingenuity, possibly the most complex machine ever built. James Gillies traces particle physics technologies from the invention of particle accelerators in the 1920s to today, and then focuses on the LHC itself. You'll get a perspective on how these tools have allowed us to make phenomenal progress in understanding the Universe, and how they have revolutionized our everyday lives.

Angels, Demons, Black Holes, and Other Myths: Demystifying the LHC

Along with humankind's natural curiosity comes a fear of the unknown. As LHC's first beam day approached in 2008, a handful of self-proclaimed experts struck up an end-of-the-world tune — and the whole world knew they were there. Like its predecessors, the Large Electron-Positron Collider (LEP) and Relativistic Heavy Ion Collider (RHIC), the LHC never posed the slightest risk to humanity. However, the "dangerous scientist" has always made for a good story and that's something that Dan Brown exploited to the full when writing Angels and Demons. Dr. Gillies will cover the fact behind the fiction of Angels and Demons and black holes at the LHC, and share the behind-the-scenes on how CERN lived with the hype.

JOHN CACIOPPO, PH.D.

The Architecture of Human Affect and Emotion: Journeys in Evaluative Space

How can knowledge of the the neural mechanisms of emotions lead to better decision making? Dr. John Cacioppo presents studies of the affect system that provide a surprising perspective on human feelings and emotions. We'll look at the complex terrain between stimulus, evaluation, and human behavioral response, finding more questions than answers — great food for thought.

Human Nature and the Need for Social Connection: Loneliness and the Social Brain

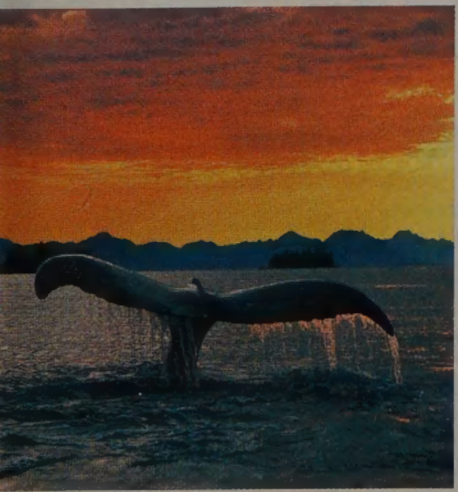
Is it fundamental human nature to serve selfish interests, or those of others? Explore how selfish genes have sculpted innate capacities for social function. We'll talk about how loneliness evolved and relates to mental and physical well being. Learn about the complex work of social neuroscience and its implications for mind, behavior and health.

Why Do I Like the Things I Like? A Look Under the Hood of Attitudes and Persuasion

How can learning about how attitudes form and persuasion works lead you to make better decisions? Can cognitive science help you be more persuasive? Look under the hood of attitudes and persuasion and see that not all attitudes are created equal. Take home new insight on snap decisions, careful consideration, and why reasonable people may disagree.

Why Is Consciousness Epiphenomenal, Or is It?

Recent work in philosophy, psychology, psychiatry, and neuroscience questions the validity of the idea of human free will. Sort through provocative questions on consciousness, perception, thought, and behavior. We'll reflect on the legal and policy implications and gain an understanding of the mechanisms that orchestrate complex human behavior and behavioral flexibility.



SCIENTIFIC AMERICAN Travel HIGHLIGHTS

INSIDER'S TOUR OF THE MUSEUM OF FLIGHT

If you love vapor trails in the wild blue yonder and the thrill of take off, join InSight Cruises in a day of fun and learning at the Museum of Flight at legendary Boeing Field near Seattle. Go behind the scenes with the Senior Curator. Explore The Boeing Company's original manufacturing plant. Get the big picture of aviation in the 3 million cubic-foot, six-story Great Gallery. An aviation historian will discuss the engineering and courage that took us from straight-wing planes to swept-wing jets. We'll do a refueling stop with a catered lunch provided by McCormick and Schmick's. After lunch, off we go into the Museum's Personal Courage Wing, followed by a talk on the development of aircraft carriers, and their technology and tactical use.

Please join us for an uplifting journey through aeronautical innovation. You may see the ubiquitous float planes of the great Northwest in a different perspective.

Lectures (60 minutes each):

Jet Propulsion and Jet Airplane Design Development

The design and development of the jet engine and the first airplanes to use them is an exciting and revealing story of personal determination in the face of bureaucratic and political obstacles before and during a World War. The remarkable transition from piston engined, straight winged airplanes to high speed swept wing jets is illustrated during this presentation. The skill and courage of the first pilots to probe the transonic speed region is summarized as a fascinating backdrop to what we take for granted as a part of modern life.

Carriers: Naval Aviation at Sea

The first attempt to take off from an aircraft carrier was in 1910, followed by a landing in 1911. This presentation will discuss the early development of aircraft carriers as well as catapults and arresting gear. Carriers played a significant role in the Pacific Theatre during World War II and in the ultimate success of the United States. Some of the most decisive carrier battles of the War will be discussed as well as what life is like aboard a "floating city".

The price is $395 and includes all of the above (7 hours), an elegant lunch at The Museum of Flight, and roundtrip transfers to/from our Seattle hotel. This tour is limited to 25 people.

Visit inside the Air Force One jet used by Presidents Eisenhower, Johnson, Kennedy, and Nixon.

Data Theft: Hackers Attack

Crooks may seek your identity, but "hacktivists" cause the blockbuster breaches

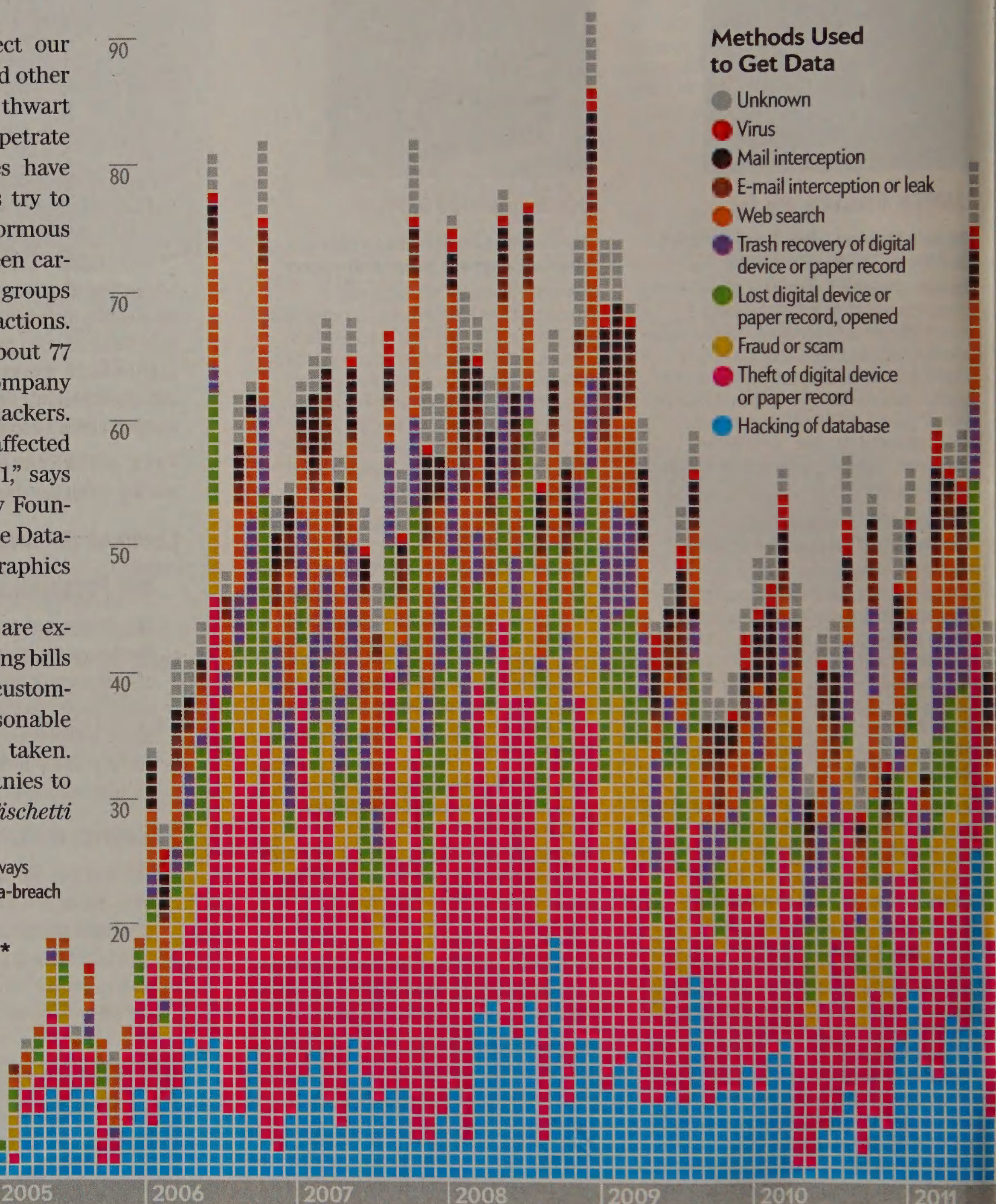
We are constantly warned to protect our passwords, Social Security numbers and other "personal identifying information" to thwart thieves who may steal laptops or perpetrate online fraud. Although such breaches have soared since 2005 (*right*) as criminals try to commit identity theft, the truly enormous breaches (*bottom*) have increasingly been carried out by "hacktivists"—individuals or groups who are angry about an organization's actions. Hackers, for example, exposed data about 77 million Sony customers after the company pursued legal action against other hackers. "More than 107 million people were affected by hacking during the first half of 2011," says Jake Kouns, CEO of the Open Security Foundation in Glen Allen, Va., which runs the DataLossDB project (the data source for graphics on this page).

Will you be informed if your data are exposed? Maybe not. Congress is considering bills that would require companies to notify customers of breaches only if there was a "reasonable risk" that personal information was taken. Right now many states require companies to disclose all breaches. —*Mark Fischetti*

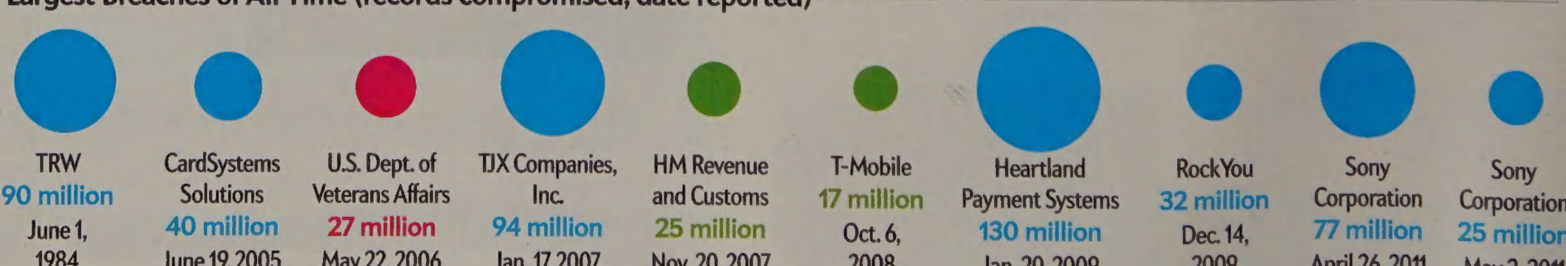
SCIENTIFIC AMERICAN ONLINE For a ranking of ways data are stolen, see ScientificAmerican.com/oct2011/data-breach

Data Breaches (incidents each month)*
■ = 1 incident

**Personal information beyond name or e-mail address, such as Social Security, financial or medical data, was exposed. Simple username or e-mail breaches are not included.*



Largest Breaches of All Time (records compromised, date reported)†



† In July data about some 35 million users on Cyworld and Nate (South Korean sites) were swiped, but the types of data are still being verified.

SOURCE: OPEN SECURITY FOUNDATION/DATALOSSDB.ORG

Graphic by Jen Christiansen